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KIRKES' HAND-BOOK OF PHYSIOLOGY

HAND-BOOK
OF
PHYSIOLOGY

By W. D. HALLIBURTON, M.D., F.R.S.
PROFESSOR OF PHYSIOLOGY, KING'S COLLEGE, LONDON.

TWENTIETH EDITION

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AUTHOR'S PREFACE TO THE SIXTH EDITION

I HAVE taken advantage of the alteration in the size of the page and of the type which Mr Murray has thought wise to adopt, to make considerable changes in the present edition. I have throughout, however, endeavoured to remember that the main object of the work is to supply students with a complete but elementary text-book. Sections which treat of what may be termed "advanced work" have therefore been made as brief as possible, and have been inserted in small print. The student on reading the book for the first time will find it best to omit these passages. When he has mastered the continuous story told in the large text, he will then be able to study what is given in small type.

During the past few years two important advanced text-books have made their appearance; one published in this country, under the editorship of Professor Schäfer, F.R.S., and the other in America, under the editorship of Professor Howell. I am much indebted to both of these for assistance in bringing this book up to date. I have also to thank Professor Schäfer for allowing me to copy several of the instructive new diagrams which have appeared in his *Essentials of Histology.*

The parts of this book which have undergone most revision are those relating to the nervous system and to the circulation of the blood. Under the latter head I have devoted some space to those elementary principles of physics which underlie what is often called hæmodynamics. Experience in teaching has shown me that although students may have previously received instruction in physics and

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HALLIBURTON'S
HAND-BOOK OF PHYSIOLOGY

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FAHRENHEIT and CENTIGRADE SCALES.

F.	C.
500°	260°
401	205
392	200
383	195
374	190
356	180
347	175
338	170
329	165
320	160
311	155
302	150
284	140
275	135
266	130
248	120
239	115
230	110
212	100
203	95
194	90
176	80
167	75
140	60
122	50
113	45
105	40·54
104	40
100	37·8
98·5	36·9
95	35
86	30
77	25
68	20
50	10
41	5
32	0
23	− 5
14	− 10
+ 5	− 15
− 4	− 20
− 13	− 25
− 22	− 30
− 40	− 40
− 76	− 60

1 deg. F. = ·54° C.
1·8 „ = 1° C.
3·6 „ = 2° C.
4·5 „ = 2·5° C.
5·4 „ = 3° C.

To convert degrees F. into degrees C., subtract 32, and multiply by $\frac{5}{9}$.

To convert degrees C. into degrees F., multiply by $\frac{9}{5}$, and add 32°.

MEASUREMENTS.

FRENCH INTO ENGLISH.

LENGTH.

1 mètre
10 décimètres
100 centimètres
1000 millimètres } = 39·37 English inches (or 1 yard and 3⅜ in.)

1 décimètre
10 centimètres
100 millimètres } = 3·937 inches (or nearly 4 inches).

1 centimétre
10 millimètres } = ·3937 or about (nearly $\frac{2}{5}$ inch).
1 millimètre = nearly $\frac{1}{25}$ inch.

Or,

One Mètre = 39·37079 inches.

(It is the ten-millionth part of a quarter of the meridian of the earth.)

1 Décimètre = 4 in.
1 Centimètre = $\frac{4}{10}$ in.
1 Millimètre = $\frac{1}{25}$ in.
Décamètre = 32·80 feet.
Hectomètre = 109·36 yds.
Kilomètre = 0·62 mile.
One inch = 2·539 Centimètres.
One foot = 3·047 Décimètres.
One yard = 0·91 of a Mètre.
One mile = 1·60 Kilomètre.

WEIGHT.

(One gramme is the *weight* of a cubic centimètre of water at 4° C. at Paris.)

1 gramme
10 décigrammes
100 centigrammes
1000 milligrammes } = 15·432349 grs. (or nearly 15½).

1 décigramme
10 centigrammes
100 milligrammes } = rather more than 1½ grain.

1 centigramme
10 décigrammes } = rather more than $\frac{3}{20}$ grain.

1 milligramme = rather more than $\frac{3}{200}$ grain.

Or,

1 Décagramme = 2 dr. 34 gr.
1 Hectogrm. = 3½ oz. (Avoir.)
1 Kilogrm. = 2 lb. 3 oz. 2 dr. (Avoir.)

A grain equals about 1·16 gram., a Troy oz. about 31 grams., a lb. Avoirdupois about ½ Kilogrm., and 1 cwt. about 50 Kilogrms.

CAPACITY.

1,000 cubic décimètres
1,000,000 cubic centimètres } = 1 cubic mètre.

1 cubic décimètre
or
1000 cubic centimètres } = 1 litre.

Or,

One Litre = 1 pt. 15 oz. 1 dr. 40.

(For simplicity, *Litre* is used to signify 1 cubic décimètre, a little less than 1 English quart.)

Décilitre (100 c.c.) = 3½ oz.
Centilitre (10 c.c.) = 2¾ dr.
Millilitre (1 c.c.) = 17 m.
Décalitre = 2¼ gals.
Hectolitre = 22 gals.
Kilolitre (cubic mètre) = 27½ bushels.

A cubic inch = 16·38 c.c.; a cubic foot = 28·315 cubic dec., and a gallon = 4·54 litres.

CONVERSION SCALE.

To convert Grammes to Ounces avoirdupois, multiply by 20 and divide by 567.

To convert Kilogrammes to Pounds, multiply by 1000 and divide by 454.

To convert Litres to Gallons, multiply by 22 and divide by 100.

To convert Litres to Pints, multiply by 88 and divide by 50.

To convert Millimètres to Inches, multiply by 10 and divide by 254.

To convert Mètres to Yards, multiply by 70 and divide by 64.

SURFACE MEASUREMENT.

1 square mètre = about 1550 sq. inches (or 10,000 sq. centimètres, or 10·75 sq. ft.)

1 sq. inch = about 6·4 sq. centimètres.
1 sq. foot = „ 930 „ „

ENERGY MEASURE.

1 kilogrammètre = about 7·24 ft. pounds.
1 foot pound = „ ·1381 kgm.
1 foot ton = „ 310 kgms.

HEAT EQUIVALENT.

1 kilocalorie = 424 kilogrammètres.

ENGLISH MEASURES.

Apothecaries Weight.

7000 grains = 1 lb.

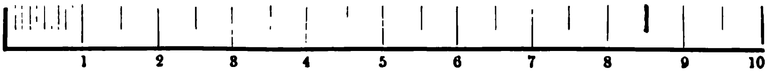
Or,

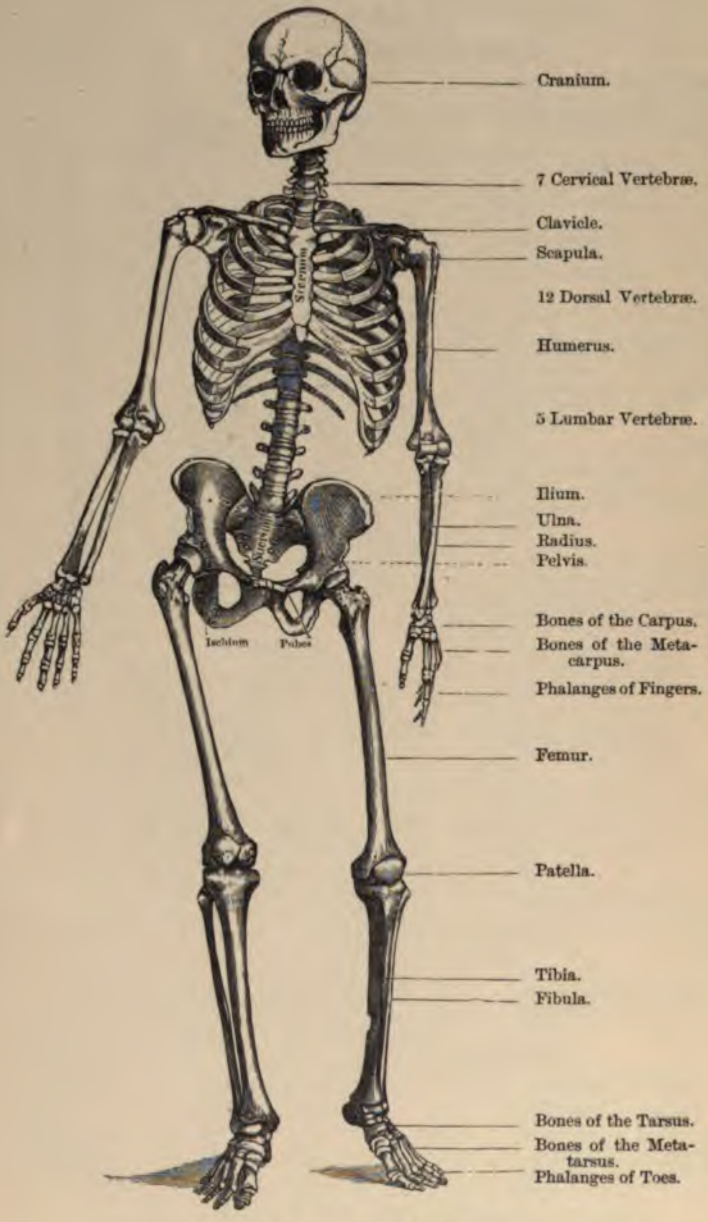
437·5 grains = 1 oz.

Avoirdupois Weight.

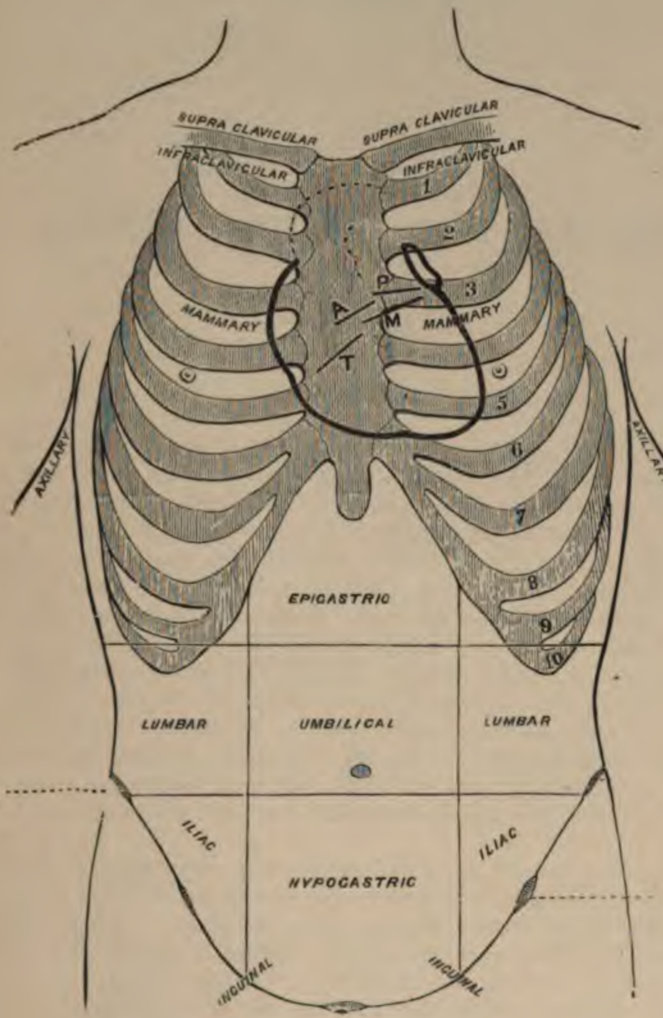
16 drams = 1 oz.
16 oz. = 1 lb.
28 lbs. = 1 quarter.
4 quarters = 1 cwt.
20 cwt. = 1 ton.

Measure of 1 décimètre, 10 centimètres, or 100 millimètres.





THE SKELETON (AFTER HOLDEN).



Highest point of Crest of the Ilium.

Anterior Superior Spine of the Ilium

Symphysis Pubis.

DIAGRAM OF THORACIC AND ABDOMINAL REGIONS.

A. Aortic Valve.
M. Mitral Valve.
P. Pulmonary Valve.
T. Tricuspid Valve.

HANDBOOK OF PHYSIOLOGY

CHAPTER I

INTRODUCTORY

Biology is the science that treats of living things, and it is divided into two main branches, which are called respectively Morphology and Physiology. *Morphology* is the part of the science that deals with the form or structure of living things, and with the problems of their origin and distribution. *Physiology*, on the other hand, treats of their functions, that is, the manner in which their individual parts carry out the processes of life. To take an instance: the eye and the liver are two familiar examples of what are called organs; the anatomist studies the structure of these organs, their shape, their size, the tissues of which they are composed, their position in the body, and the variations in their structure met with in different parts of the animal kingdom. The physiologist studies their uses, and seeks to explain how the eye fulfils the function of vision, and how the liver forms bile, and ministers to the needs of the body in other ways.

Each of these two great branches of biological science can be further subdivided according as to whether it deals with the animal or the vegetable kingdom; thus we get vegetable physiology and animal physiology. Human Physiology is a large and important branch of animal physiology, and to the student of medicine is obviously the portion of the science that should interest him most. In order to understand morbid or pathological processes it is necessary that the normal or physiological functions should be learnt first. Physiology is not a study which can be put aside and forgotten when a certain examination has been passed; it has a most direct and intimate bearing in its application to the scientific and successful investigation of disease. It will be my endeavour throughout the subsequent pages of this book to point out from time to time the practical relationships between physiology and pathology.

Human physiology will be our chief theme, but it is not a portion of the great science that can be studied independently of its other portions. Thus, many of the experiments upon which our knowledge of human physiology rests have been performed principally on certain of the lower animals. In order to obtain a wide view of vital processes it will be occasionally necessary to go still further afield, and call the science of vegetable physiology to our assistance.

The study of physiology must go hand in hand with the study of anatomy. It is impossible to understand how the body or any part of the body acts unless we know accurately the structure of the organs under consideration. This is especially true for that portion of anatomy which is called Microscopic Anatomy or Histology. Indeed, so close is the relationship between minute structure and function that in this country it is usual for the teacher of physiology to be also the teacher of histology. Another branch of anatomy, namely, Embryology, or the process of growth from the ovum, falls also to some extent within the province of the physiologist.

But physiology is not only intimately related in this way to its sister science anatomy, but the sciences of chemistry and physics must also be considered. Indeed, physiology has been sometimes defined as the application of the laws of chemistry and physics to life. That is to say, the same laws that regulate the behaviour of the mineral or inorganic world are also to be found operating in the region of organic beings. If we wish for an example of this we may again go to the eye; the branch of physics called optics teaches us, among other things, the manner in which images of objects are produced by lenses; these same laws regulate the formation of the images of external objects upon the sensitive layer of the back of the eye by the series of lenses in the front of that organ. An example of the application of chemical laws to living processes is seen in digestion; the food contains certain chemical substances which are acted on in a chemical way by the various digestive juices in order to render them of service to the organism.

The question arises, however, is there anything else? Are there any other laws than those of physics and chemistry to be reckoned with? Is there, for instance, such a thing as "vital force"? It may be frankly admitted that physiologists at present are not able to explain all vital phenomena by the laws of the physical world; but as knowledge increases it is more and more abundantly shown that the supposition of any special or vital force is unnecessary; and it should be distinctly recognised that when, in future pages, it is necessary to allude to vital action, it is not because we believe in any specific vital energy, but merely because the phrase is a convenient one for expressing something that we do not fully understand, something that cannot at present be brought into line with the physical and chemical forces that operate in the inorganic world.

Physiology proper may be conveniently divided into three main branches:—

1. Chemical physiology; or the application of chemistry to living processes.
2. Physical physiology; or the application of physics to living processes.
3. The physiology of the nervous system where the application of such laws is at present extremely difficult.

But just as there is no hard-and-fast line between physiology and its allies pathology, anatomy, physics, and chemistry, so also there is no absolute separation between its three great divisions; physical, chemical, and so-called vital processes have to be considered together.

Physiology is a comparatively young science. Though Harvey more than three hundred years ago laid the foundation of our science by his discovery of the circulation of the blood, it is only during the last half-century that active growth has occurred. The reasons for this recent progress come under two headings: those relating to observation and those relating to experiment.

The method of observation consists in accurately noting things as they occur in nature; in other words, the knowledge of anatomy must be accurate before correct deductions as to function are possible. The instrument by which such correct observations can be made is, *par excellence*, from the physiologist's standpoint, the microscope, and it is the extended use of the microscope, and the knowledge of minute anatomy resulting from that use, which has formed one of the greatest stimuli to the successful progress of physiology during the last sixty years.

But important as observation is, it is not the most important method; the method of experiment is still more essential. This consists, not in being content with mere reasonings from structures or occurrences seen in nature, but in producing artificially changed relationships between the structures, and thus causing new combinations that if one had waited for Nature herself to produce might have been waited for indefinitely. Anatomy is important, but mere anatomy has often led people astray when they have tried to reason how an organ works from its structure only. Experiment is much more important; that is, one tests one's theories by seeing whether the occurrences actually take place as one supposes; and thus the deductions are confirmed or corrected. It is the universal use of this method that has made physiology what it is. Instead of sitting down and trying to reason out how the living machine works, physiologists have actually tried the experiment, and so learnt much more than could possibly have been gained by mere cogitation. Many experiments involve the use of living animals, but the discovery of anæsthetics, which renders such experiments painless, has got rid of any objection to experiments on the score of pain.

We must next proceed to an examination of the general structure of the body, and an explanation of some of the technical terms which will frequently be used hereafter.

The adult body consists of a great number of different parts; and each part has its own special work to do. Such parts of the body are called **organs**. Each organ does not only its own special work, but acts in harmony with other organs. This relationship between the organs enables us to group them together into what are termed **systems**. Thus, we have the *circulatory system*, that is, the group of organs (heart, arteries, veins, etc.) concerned in the circulation of the blood; the *respiratory system*, that is, the group of organs (air passages, lungs, etc.) concerned in the act of breathing; the *digestive system*, which deals with the digestion of food; the *excretory system*, with the getting rid of waste products; the *muscular system*, with movement; and the *skeletal system*, with the support of the softer parts of the body. Over and above all these is the *nervous system* (brain, spinal cord, nerves), the great master system of the body which presides over, controls, and regulates the functions of the other systems.

If we proceed still further on our anatomical analysis, and take any organ, we see that it consists of various textures, or, as they are called, **elementary tissues**. Just as one's garments are made up of textures (cloth, lining, buttons, etc.), so each organ is composed of corresponding tissues. The elementary tissues come under the following four headings:—

1. Epithelial tissues.
2. Connective tissues.
3. Muscular tissues.
4. Nervous tissues.

Each of these is again divisible into sub-groups.

Suppose we continue our anatomical analysis still further, we find that the individual tissues are built up of structures which require the microscope for their accurate study. Just as the textures of a garment are made up of threads of various kinds, so also in many of the animal tissues we find threads or *fibres*, as they are called. But more important than the threads are little masses of living material. Just as the wall of a house is made up of bricks united by cement, so the body walls are built of extremely minute living bricks, united together by different amounts of cementing material. Each one of these living units is called a **cell**.

Some of the tissues already enumerated consist of cells with only very little cement material binding them together; this, for instance, is seen in the epithelial tissues; but in other tissues, particularly the connective tissues which are not so eminently living as the rest, the amount of cement or **intercellular material** is much greater, and in this it is that the fibres are developed that confer the necessary strength upon these binding tissues.

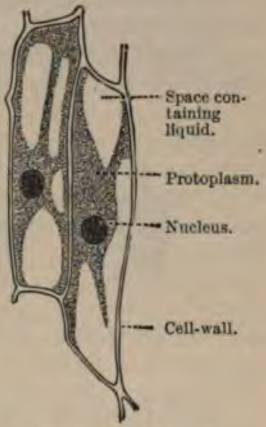


FIG. 1.—Vegetable cells.

If, instead of going to the adult animal, we look at the animal in its earliest stage of development, the ovum, we find that it consists of a single little mass of living material, a single cell. As development progresses it becomes an adherent mass of cells. In the later stages of development various tissues become differentiated from each other by the cells becoming grouped in different ways, by alterations in the shape of the cells, by deposition of intercellular matter between the cells, and by chemical changes in the living matter of the cells themselves. Thus in some situations the cells are grouped into the various epithelial linings; in others the cells become elongated and form muscular fibres; and in others, as in the connective tissues, there is a preponderating amount of intercellular material which may become permeated with fibres, or be the seat of the deposition of calcareous salts, as in bone. Instances of chemical changes in the cells themselves are seen on the surface of the body where the superficial layers of the epidermis become horny; in the mucous glands, where they become filled with mucin, and in adipose tissue, where they become charged with fat.

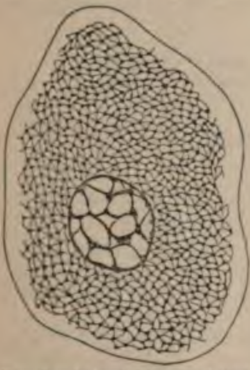


FIG. 2.—Animal cell consisting of protoplasm containing a nucleus.

The term cell was first used by botanists; in the popular sense of the word a cell is a space surrounded by a wall, as the cell of a prison, or the cell of a honeycomb. In the vegetable cell there is a wall made of the starch-like material called cellulose, within this is the living matter, and a number of large spaces or vacuoles filled with a watery fluid. The use of the term cell by botanists was therefore completely justified.

But the animal cell is different; as a rule, it has no cell-wall, and no vacuoles. It is just a little naked lump of living material. This living material is jelly-like in consistency, possessing the power of movement, and the name **protoplasm** has been bestowed on it.

Somewhere in the protoplasm of all cells, generally near the middle in animal cells, is a roundish structure of more solid consistency than the rest of the protoplasm, called the **nucleus**.

An animal cell may therefore be defined as a *mass of protoplasm containing a nucleus.*

The simplest animals, like the amœbæ, consist of one cell only; the simplest plants, like bacteria, torulæ, etc., consist of one cell only.

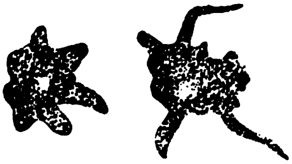


FIG. 3.—Amœbæ; unicellular animals.

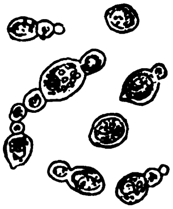


FIG. 4.—Cells of the yeast plant in process of budding; unicellular plants.

Such organisms are called unicellular. In the progress of their life history the cell divides into two; and the two new cells separate and become independent organisms, to repeat the process later on.

In the case of the higher animals and plants, they are always unicellular to start with, but on dividing and subdividing the resulting cells stick together and subsequently become differentiated and altered in the manner already indicated. In spite of these changes, the variety of which produces the great complexity of the adult organism, there are certain cells which still retain their primitive structure; notable among these are the white corpuscles of the blood.

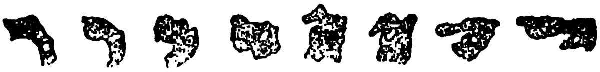


FIG. 5.—Human colourless blood-corpuscle, showing its successive changes of outline within ten minutes when kept moist on a warm stage. (Schofield.)

It would appear at first sight an easy problem to distinguish between a living thing, and one which is not living. The principal signs of life are the following:—

1. Irritability; that is the property of responding by some change under the influence of an external agent or stimulus. The most obvious of these changes is movement (amœboid movement, ciliary movement, muscular movement, etc.).

2. Power of assimilation, that is, ability to convert into protoplasm the nutrient material or food which is ingested.

3. Power of growth; this is a natural consequence of the power of assimilation.

4. Power of reproduction; this is a variety of growth.
5. Power to excrete; to give out waste materials, the products of other activities.

It should, however, be recognised that certain of these five characteristics may be absent or latent, and yet the object may be living. For instance, power of movement is absent in many vegetable structures; certain seeds and spores can be dried and kept for many years in an apparently dead condition, and yet will sprout and grow when placed in appropriate surroundings.

Of all the signs of life, those numbered 2 and 5 in the foregoing table are the most essential. Living material is in a continual state of unstable chemical equilibrium, building itself up on the one hand, breaking down on the other; the term used for the sum total of these intra-molecular rearrangements is **metabolism**. The chemical substances in the protoplasm which are the most important from this point of view are the complex nitrogenous compounds called *Proteids.* So far as is at present known, proteid material is never absent from living substance, and is never present in any thing else but that which is alive or has been formed by the agency of living cells. It may therefore be stated that **Proteid Metabolism** is the most essential characteristic of vitality.

CHAPTER II

THE ANIMAL CELL

An animal cell is usually of microscopic dimensions, in the human body varying from $\frac{1}{300}$ to $\frac{1}{3000}$ of an inch in diameter.

It consists of—

1. *Protoplasm.* This makes up the main substance of the cell.

2. *Nucleus:* a vesicular body within the protoplasm, generally situated near the centre of the cell.

3. *Centrosome and attraction sphere:* these are contained within the protoplasm, near the nucleus.

These three portions demand separate study.

Protoplasm.

Until recent years, protoplasm was supposed to be a homogeneous material entirely destitute of structure, though generally containing minute granules of solid consistency, or globules (vacuoles) containing a watery fluid.

It has, however, now been shown with high powers of the microscope that in many cells the protoplasm consists of two parts, a fine network of fibrillæ in which the more fluid and apparently structureless portion of the protoplasm is contained. (See figs. 2 and 6.)

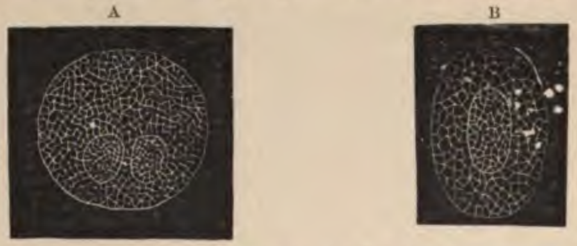


Fig. 6.—(A.) A colourless blood-corpuscle showing the intra-cellular network, and two nuclei with intra-nuclear network.
(B.) Coloured blood-corpuscle of newt showing the intra-cellular network of fibrils. Also oval nucleus composed of limiting membrane and fine intra-nuclear network of fibrils. × 800. (Klein and Noble Smith.)

The network or spongework is called the **reticulum** or **spongioplasm,** and the more fluid portion in its meshes the **enchylema** or **hyaloplasm.**

In order to study the microscopic structure of such transparent objects as cells, it is necessary to have recourse to various methods of fixing and staining. When one sees certain appearances after such treatment of the cells, the question arises whether they may not be due to the action of the reagents employed. Appearances which are undoubtedly produced artificially in this way are generally spoken of as *artifacts*. The network just described is regarded by some observers as an artifact, but it is impossible at present to state this positively. Hardy, in particular, has shown that a film of any colloidal substance like gelatin will, when it sets, present the appearance of a network, and he regards it as probable that the network seen in cells may be due to a similar setting or coagulation of the protoplasm which occurs either when the cell dies, or is fixed by hardening reagents. Bütschli regards the spongioplasm as the optical effect of a honeycomb or froth-like structure. There are numerous other views.

The granules in protoplasm are partly thickened portions of the spongioplasm, but in addition to this there appear to be free granules, some fatty in nature (staining black with osmic acid), some composed of the substance called glycogen or animal starch (staining reddish-brown with iodine), and sometimes in a few unicellular animals they consist of inorganic (calcareous) matter. But by far the most constant and abundant of the granules are like the main substance of the protoplasm, proteid or albuminous in composition. In all probability the proteid granules are actual constituents of the protoplasm. Substances stored within the protoplasm, like pigment granules, fat globules, fluid in vacuoles, and glycogen, are spoken of as *cell-contents* or *paraplasm.*

The chemical structure of protoplasm can only be investigated after the protoplasm has been killed. The substances it yields are (1) **Water**; protoplasm is semifluid, and at least three-quarters of its weight, often more, are due to water. (2) **Proteids.** These are the most constant and abundant of the solids. A proteid or albuminous substance consists of carbon, hydrogen, nitrogen, oxygen, with sulphur and phosphorus in small quantities only. In nuclein, a proteid-like substance found in the nuclei of cells, phosphorus is more abundant. The proteid obtained in greatest abundance in the cell protoplasm is called a **nucleo-proteid**; that is to say, it is a compound containing varying amounts of this material nuclein with proteid. White of egg is a familiar instance of an albuminous substance or proteid, and the fact (which is also familiar) that this sets into a solid on boiling will serve as a reminder that the greater number of the proteids found in nature have a similar tendency to coagulate under the influence of heat and other agencies. (3) Various other substances occur in smaller proportions, the most constant of which are **lecithin,** a phosphorised fat; **cholesterin,** a monatomic alcohol; and **inorganic salts**, especially phosphates and chlorides of calcium, sodium, and potassium.

The large quantity of water present should be particularly noted; the student when first shown diagrams of the reticulum in protoplasm is apt to imagine that it consists of a firm solid, like a system of wires pervading a jelly. The reticulum is only slightly more solid than the hyaloplasm.

The Nucleus.

In form the nucleus is generally round or oval, but it may have in some cases an irregular shape, and in other cases there may be more than one nucleus in a cell.

The nucleus exercises a controlling influence over the nutrition and subdivision of the cell; any portion of a cell cut off from the nucleus undergoes degenerative changes.

A nucleus consists of four parts—

1. *The nuclear membrane*, which encloses it.
2. *A network* of fibres in appearance like the spongioplasm of the protoplasm but on a larger scale; that is to say, the threads of which it is composed are much coarser and much more readily seen. The name **chromoplasm** has been given to this network.
3. *The nuclear sap or matrix*, a more fluid and homogeneous substance which occupies the interstices of the spongework of chromoplasm.
4. *Nucleoli;* these are of two principal varieties; some are knots or thickened portions of the network (pseudo-nucleoli), and others, the true nucleoli, float freely in the nuclear sap.

These four parts of the nucleus are represented in the next diagram.

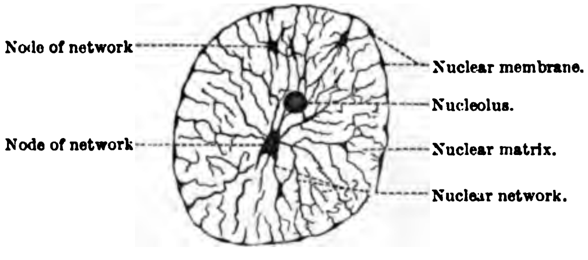


FIG. 7.—The resting nucleus—diagrammatic. (Waldeyer.)

The next figure (fig. 8) gives a view of the nucleus, according to the researches of Rabl. He considers that the fibres of the network may be divided into thick fibres which he terms primary, and thinner connecting branches which he terms secondary (shown only on the right-hand side of the figure). This observer also supposes that the primary fibres have the looped arrangement depicted in the diagram.

In the investigation of microscopic objects, a histologist is nearly always obliged to use staining agents; the extremely thin objects he examines are so transparent that, without such stains, much of the structure would be invisible. If such dyes as hæmatoxylin or safranin are employed, it is the nucleus which becomes most deeply stained, and thus stands out on the lighter background of the protoplasm.

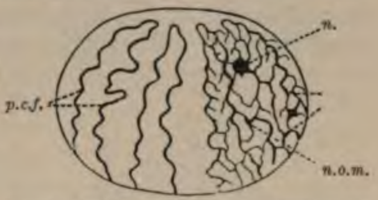


Fig. 8.—Diagram of nucleus showing the arrangement of chief chromatic filaments. Viewed from the side, the polar end being uppermost. *p.c.f.*, primary chromatic filaments; *n.*, nucleolus; *n.o.m.*, node of meshwork. (Rabl.)

But the whole nucleus does not stain equally deeply; it is the chromoplasmic filaments and the nucleoli which have most affinity for the stain, while the nuclear sap is comparatively unaffected. Hence the terms *chromatin* and *achromatin* originally introduced by Fleming. The membrane, the network, and the nucleoli are composed of chromatic substance or chromatin; it is so called not because it has any colour in the natural state, but because it has an affinity for colours artificially added to it. For a corresponding reason, achromatin or achromatic substance is the name given to the substances which make up the nuclear sap.

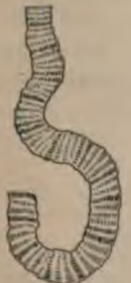


Fig. 9.—Part of a chromoplasmic filament, greatly magnified. (Carnoy.)

Balbiani showed that the chromoplasmic filaments are apparently transversely marked into alternate dark and light bands; this is due to the existence of minute highly refracting particles imbedded in regular series in a clear homogeneous and unstainable matrix (see fig. 9). The term *chromatin* should properly be restricted to these particles. These particles have special affinity for basic dyes like methyl green, and safranin.

Coming next to the chemical composition of the nucleus, it is found to consist principally of proteid and proteid-like substances. The nuclei of cells may be obtained by subjecting the cells to the action of artificial gastric juice; the protoplasm is nearly entirely dissolved, but the nuclei resist the solvent action of the juice. No doubt the nuclei contain several chemical compounds, but the only one of which we have any accurate knowledge has been termed *nuclein*, and this is identical with the substance called *chromatin* by histologists. It is soluble in alkalis, but precipitated by acids; it is different from a proteid, as it contains in addition to carbon, nitrogen, oxygen, hydrogen, and sulphur, an enormous quantity (7 to 8 per cent. or even more) of phosphorus in its molecule. In many cases nucleins contain iron also.

The Attraction Sphere.

Recent research has shown that, in addition to the nucleus and protoplasm, most if not all living cells contain another structure; it consists of a minute particle called a "*centrosome*," which has an attractive influence on protoplasmic fibrils and granules in its neighbourhood, the whole appearance produced being called an *attraction sphere* (fig. 10).

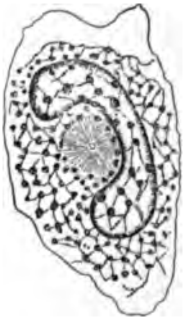


FIG. 10.—A cell (white blood-corpuscle) showing its attraction sphere. In this, as in most cases, the attraction sphere lies near the nucleus. (Schäfer.)

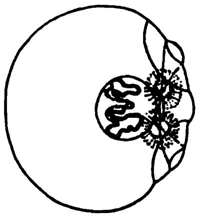


FIG. 11.—Ovum of the worm Ascaris, showing a twin attraction sphere. The nucleus with its contorted filament of chromoplasm is represented, but the protoplasm of the cell is not filled in. (v. Beneden.)

It is most prominent in cells which are dividing or about to divide. The centrosome, and then the attraction sphere, become double (fig. 11). In all probability the centrosome gives the primary impulse to cell-division. Some cells, like the giant cells of red marrow, contain numerous centrosomes.

Protoplasmic Movement.

A cell possesses the power of *breathing*, that is, taking in oxygen; of *nutrition*, of building itself up from food materials; and of *excretion*, or the getting rid of waste material. But the most obvious physiological characteristic of most cells is their power of *movement*.

When an amœba is observed with a high power of the microscope, it is found to consist of an irregular mass of protoplasm containing one or more nuclei, the protoplasm itself being more or less granular and vacuolated. If watched for a minute or two, an irregular projection is seen to be gradually thrust out from the main body and retracted; a second mass is then protruded in another direction, and gradually the whole protoplasmic substance is, as it were, drawn into it. The Amœba thus comes to occupy a new position, and when this is repeated several times we have locomotion in a definite direction, together with a continual change of form. These movements, when observed in other cells, such as the colourless blood-corpuscles of higher animals (fig. 13), in the branched corneal cells of the frog and elsewhere, are hence termed *amœboid.* The projections which are alternately protruded and retracted are called *pseudopodia.*

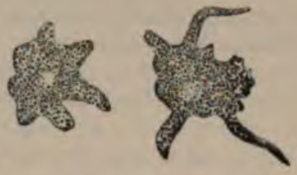


FIG. 12.—Amœbæ.

A *streaming* movement is not infrequently seen in certain of the protozoa, in which the mass of protoplasm extends long and fine processes, themselves very little movable, but upon the surface of which freely-moving or streaming granules are seen. A *gliding* movement has also been noticed in certain animal cells; the motile part of the cell is composed of protoplasm bounding a central and more compact mass; by means of the free movement of this layer, the cell may be observed to move along.

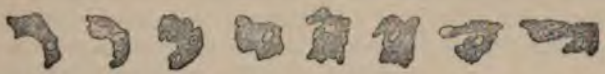


FIG. 13.—Human colourless blood-corpuscle, showing its successive changes of outline within ten minutes when kept moist on a warm stage. (Schofield.)

In vegetable cells the protoplasmic movement can be well seen in the hairs of the stinging-nettle and Tradescantia and the cells of Vallisneria and Chara; it is marked by the movement of the granules nearly always imbedded in it. For example, if part of a hair of Tradescantia (fig. 15) be viewed under a high magnifying power,

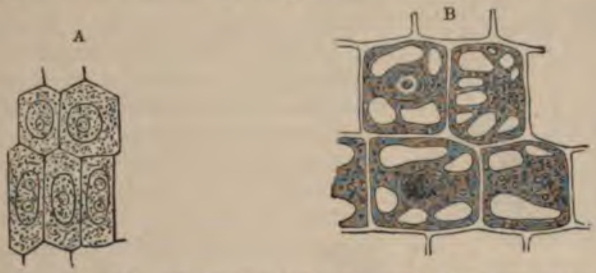


FIG. 14.—(A.) Young vegetable cells, showing cell-cavity entirely filled with granular protoplasm enclosing a large oval nucleus, with one or more nucleoli.
(B.) Older cells from same plant, showing distinct cellulose-wall and vacuolation of protoplasm.

streams of protoplasm containing crowds of granules hurrying along, like the foot-passengers in a busy street, are seen flowing steadily in definite directions, some coursing round the film which lines the interior of the cell-wall, and others flowing towards or away from the irregular mass in the centre of the cell-cavity. Many of these streams of protoplasm run together into larger ones and are lost in the central mass, and thus ceaseless variations of form are produced. The movement of the protoplasmic granules to or from the periphery is sometimes called vegetable *circulation*, whereas the movement of the protoplasm round the interior of the cell is called *rotation*.

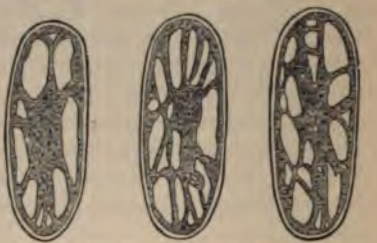


FIG. 15.—Cell of Tradescantia drawn at successive intervals of two minutes.—The cell-contents consist of a central mass connected by many irregular processes to a peripheral film, the whole forming a vacuolated mass of protoplasm, which is continually changing its shape. (Schofield.)

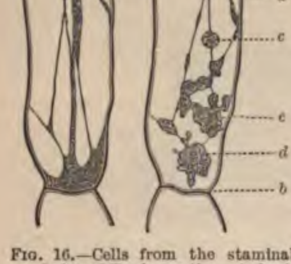


FIG. 16.—Cells from the staminal hairs of Tradescantia. *A*, fresh in water; *B*, the same cell after slight electrical stimulation; *a*, *b*, region of stimulation; *c*, *d*, clumps and knobs of contracted protoplasm. (Kühne.)

The first account of the movement of protoplasm was given by Rösel in 1755, as occurring in a small Proteus, probably a large freshwater amœba. His description was followed twenty years later by Corti's demonstration of the rotation of the cell sap in Characeæ, and in the earlier part of last century by Meyer in Vallisneria, 1827, and by Robert Brown, 1831, in "Staminal Hairs of Tradescantia." Then came Dujardin's description of the granular streaming in the pseudopodia of Rhizopods; movements in other animal cells were described somewhat later (Planarian eggs, v. Siebold, 1841; colourless blood-corpuscles, Wharton Jones, 1846).

There is no doubt that the protoplasmic movement is essentially the same thing in both animal and vegetable cells. But in vegetable cells the cell-wall obliges the movement to occur in the interior, while in the naked animal cells the movement results in an external change of form.

Although the movements of amœboid cells may be loosely described as spontaneous, yet they are produced and increased under the action of external agencies which excite them, and which are therefore called *stimuli*, and if the movement has ceased for the time, as is the case if the temperature is lowered beyond a certain point, movement may be set up by raising the temperature. Again, contact with foreign bodies, gentle pressure, certain salts, and electricity, produce or increase the movement in the amœba. The protoplasm is, therefore, sensitive or irritable to stimuli, and shows its irritability by movement or contraction of its mass.

The effects of some of these stimuli may be thus further detailed:—

a. Changes of temperature.—Moderate heat acts as a stimulant: the movement stops when the temperature is lowered near the freezing-point or raised above 40° C. (104° F.); between these two points the movements increase in activity; the optimum temperature is about 37° to 38° C. Though cold stops the movement of protoplasm, exposure to a temperature even below 0° C. does not prevent its reappearance if the temperature is raised; on the other hand, prolonged exposure to a temperature of 42°-45° C. altogether kills the protoplasm and causes it to enter into a condition of coagulation or *heat rigor*. We have already seen that proteids, the most abundant constituents of protoplasm, are coagulated by heat.

b. Chemical stimuli.—Distilled water first stimulates then stops amœboid movement, for by imbibition it causes great swelling and finally bursting of the cells. In some cases, however (myxomycetes), protoplasm can be almost entirely dried up, but remains capable of renewing its movement when again moistened. Dilute salt solution and very dilute alkalis stimulate the movements temporarily. Acids or strong alkalis permanently stop the movements: ether, chloroform, veratrine and quinine also stop it for a time.

Movement is suspended in an atmosphere of hydrogen or carbonic acid, and resumed on the admission of air or oxygen; complete withdrawal of oxygen will after a time kill protoplasm.

c. Electrical.—Weak currents stimulate the movement, while strong currents cause the cells to assume a spherical form and to become motionless.

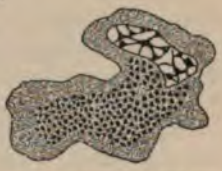


FIG. 17.—An Amœboid corpuscle of the newt killed by instantaneous application of steam, showing the appearance of the pseudopodia. (After Schäfer, "Quain's Anatomy.")

The amœboid movements of the colourless corpuscles of the blood may be readily seen when a drop of blood from the finger is mixed with salt solution, and examined on a warm stage with the microscope. If a pseudopodium of such a corpuscle is observed under a high power, it will be seen to consist of hyaloplasm, which has flowed out of its spongy home, the reticulum. Later, however, a portion of the reticular part of the protoplasm may enter the pseudopodium. The cells may be fixed by a jet of steam allowed to play for a moment on the surface of the cover glass. The next figure illustrates one fixed in this way.

The essential act in the protrusion of a pseudopodium is the flowing of the hyaloplasm out of the spongioplasm; the retraction of the pseudopodium is a return of the hyaloplasm to the spongioplasm. The spongioplasm has an irregular arrangement with openings in all directions, so that the contractility of undifferentiated cells may exhibit itself towards any point of the compass.

The relation of cells to various forms of stimulus has been recently very extensively studied. Various forms of unicellular organisms have been used in these experiments, and the stimuli employed have been chemical, thermal, light, electric currents, and so forth. If the cell moves towards the source of attraction, the term *positive taxis* is employed; if it is repelled, *negative taxis*. The words, chemo-taxis, thermo-taxis, photo-taxis, galvano-taxis, etc., indicate the kind of stimulus investigated.

Cell Division.

A cell multiplies by dividing into two; each remains awhile in the resting or, more correctly, non-dividing condition, but later it grows and subdivides, and the process may be repeated indefinitely.

The supreme importance of the cell, the growth of the body from cells, and the fact that cells are the living units of the organism, were first established in the vegetable world by Schleiden, and extended to the animal kingdom by Theodor Schwann. The ideas of physiologists depending on this idea are grouped together as cellular physiology, which under the guidance of Virchow was extended to pathology also: Virchow expressed the doctrine now so familiar as to be almost a truism in the terse phrase *omnis cellula e cellula* (every cell from a cell).

The division of a cell is preceded by division of its nucleus. Nuclear division may be either (1) *simple or direct*, which consists in the simple exact division of the nucleus into two equal parts by constriction in the centre, which may have been preceded by division of the nucleoli; or (2) *indirect*, which consists in a series of changes which goes on in the arrangement of the nuclear reticulum, resulting in the exact division of the chromatic fibres into two parts, which form the chromoplasm of the daughter nuclei.

The changes in the nucleus during indirect division constitute *karyokinesis* (κάρυον, a kernel), or *mitosis* (μίτος, a thread), and direct division is called *amitotic* or *akinetic* (κίνησις, movement). It is now believed that the mitotic nuclear division is all but, though not quite, universal. Somewhat different accounts of the stages of the nuclear division have been given by different authorities, according to the kind of cell in which the nuclear changes have been studied. The following figure (fig. 18) shows some of the typical stages of karyokinesis as observed by Klein:—

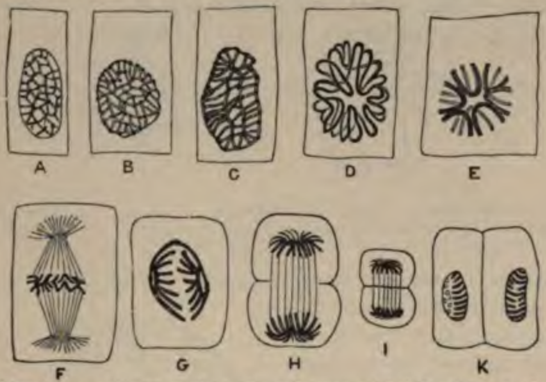


FIG. 18.—Karyokinesis. A, ordinary nucleus of a columnar epithelial cell; B, C, the same nucleus in the stage of *convolution*; D, *the wreath or rosette* form; E, the *aster*, or single star; F, a nuclear spindle from the Descemet's endothelium of the frog's cornea; G, H, I, diaster; K, two daughter nuclei. (Klein.)

The process may be divided into the following stages:—

1. The non-dividing nucleus (fig. 19.)

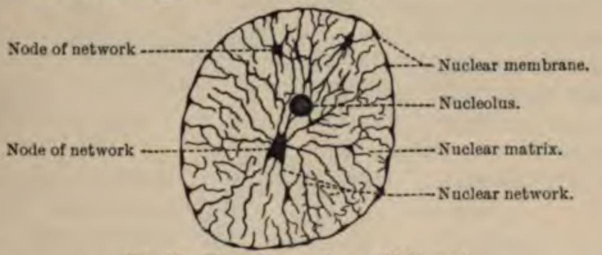


FIG. 19.—The resting nucleus. (Waldeyer.)

2. The spirem or skein stage: the nucleoli dissolve, the secondary fibres disappear, and the primary loops running from polar to antipolar regions remain (figs. 8, 20). In some cells there is at first one long, much twisted thread, which subsequently breaks up into segments. The loops are called *chromosomes.*

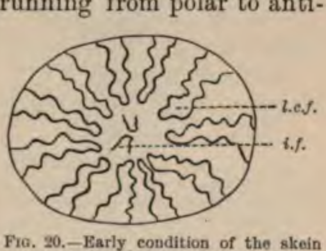


FIG. 20.—Early condition of the skein stage viewed at the polar end. *l. c. f.*, looped chromatic filament. *i. f.*, irregular filament. (Rabl.)

3. Each loop becomes less convoluted and splits longitudinally into two sister threads, and the achromatic spindle appears (fig. 21, A and B).

4. The equatorial stage; monaster. The nucleus has now two poles, those of the spindle; and at each pole there is a polar corpuscle or centro-

some. The division of the centrosome of the original cell, and then of the attraction sphere into two, usually precedes the commencement of changes in the nucleus; the two attraction spheres become prominent in cell division, and the connecting achromatic spindle is probably also formed from them or from the achromatic material of the nucleus.

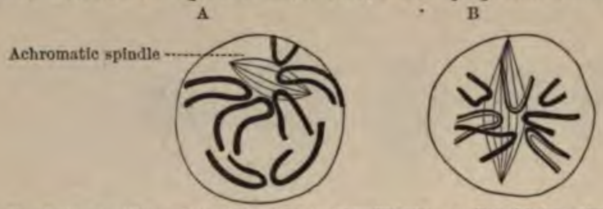


FIG. 21.—Later condition of the skein stage in karyokinesis. A. The thicker primary fibres or chromosomes become less convoluted and the achromatic spindle appears. B. The chromosomes split into two and the achromatic spindle becomes longitudinal. (Waldeyer.)

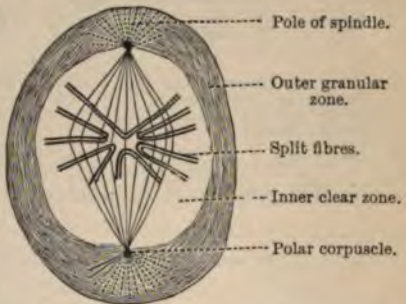


FIG. 22.—Monaster stage of karyokinesis. (Waldeyer.)

At this stage the nuclear membrane is lost, and thus cell protoplasm and nuclear sap become continuous; the protoplasm immediately around the nucleus is clear; outside this is a granular zone, and here the granules are arranged radially from the polar corpuscles. The star-like arrangement of these granules is much better marked in embryonic cells, indeed the lines present very much the appearance of fibrils (see fig. 23).

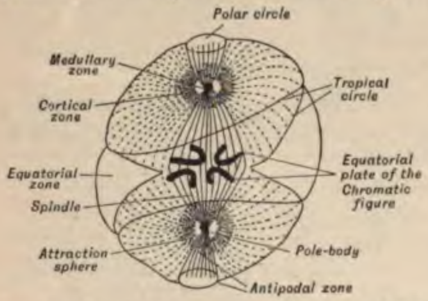


FIG. 23.—Ovum of the worm Ascaris in process of division. The attraction spheres are at opposite ends of the ovum; at the equator of the spindle which unites them, four chromosomes are seen. The protoplasm of the ovum, except in the equatorial zone of the cell, is arranged in lines radiating from the centre (centrosome) of the attraction sphere. (Waldeyer.)

The V-shaped *chromosomes* sink to the equator of the spindle, and arrange themselves so as to project horizontally from it.

In cells which are the result of the sexual process, the number of chromosomes is always even, an equal number being contributed by each sex.

The number of chromosomes varies with the species from four to twenty-four; in man the number is sixteen.

5. *The stage of metakinesis.* The sister threads separate, one set going towards one pole, and the other to the other pole of the spindle (fig. 24): these form the two daughter nuclei. The chromosomes are probably pulled into their new position by the contraction of the spindle fibres attached to them.

6. Each daughter nucleus goes backwards through the same series of changes; the diaster or double star is followed by the dispirem or double skein, until at last two resting nuclei are obtained (fig. 25).

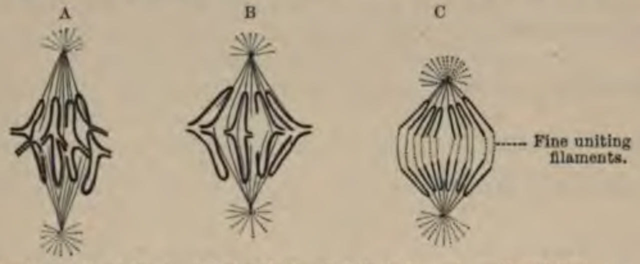


FIG. 24.—Metakinesis. A. Early stage. B. Later stage. C. Latest stage—formation of diaster. B. and C. show how the sister threads disentangle themselves from one another. (Waldeyer.)

A new membrane forms around each daughter nucleus, the spindle atrophies, and the attraction sphere becomes less prominent. The division of the cell protoplasm into two parts around the two nuclei begins in the diaster stage, and is complete in the stage represented in fig. 25.

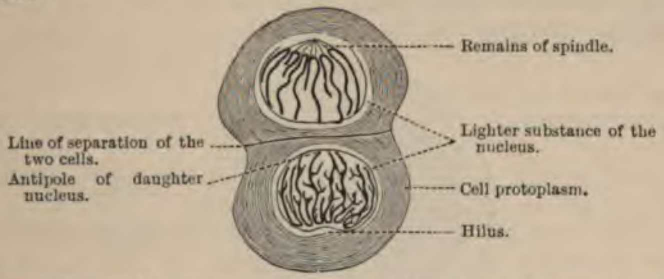

Remains of spindle.
Line of separation of the two cells.
Lighter substance of the nucleus.
Antipole of daughter nucleus.
Cell protoplasm.
Hilus.

FIG. 25.—Final stages of karyokinesis. In the lower daughter nucleus the changes are still more advanced than in the upper. (Waldeyer.)

The karyokinetic process has been watched in all its stages by more than one observer. The time occupied varies from half an hour to three hours; the details, however, must be studied in hardened and appropriately stained specimens. They are most readily seen in cells with large nuclei, such as occur in the epidermis of amphibians.

The process varies a good deal in different animal and vegetable cells; such as in the number of chromosomes, and the relative importance of the different stages. All attempted here has been to give an account of a typical case. The phases may be summarised in a tabular way as follows (from "Quain's Anatomy"):—

Network or Reticulum	1. Resting condition of mother nucleus (fig. 19).
Skein or Spirem	2. Close skein of fine convoluted filaments (fig. 20). 3. Open skein of thicker filaments. Spindle appears (fig. 21 A).
Cleavage	4. Movement of V-shaped chromosomes to middle of nucleus, and each splits into two sister threads (fig. 21 B).
Star or Monaster	5. Stellate arrangement of V filaments at equator of spindle (fig. 22).
Divergence or Metakinesis	6. Separation of cleft filaments and movement along fibres of spindle (fig. 24 A and B).
Double Star or Diaster	7. Conveyance of V filaments towards poles of spindle (fig. 24 C).
Double Skein or Dispirem	8. Open skein in daughter nuclei. 9. Close skein in daughter nuclei (fig. 25).
Network or Reticulum	10. Resting condition of daughter nuclei (fig. 25).

The Ovum.

The ovary is an organ which produces ova.

An ovum is a simple animal cell; its parts are seen in the next diagram.

It is enclosed in a membrane called the zona pellucida or vitelline membrane. The body of the cell is composed of protoplasm loaded with granules of food material, called the yolk or vitellus. The nucleus and nucleolus are sometimes still called by their old names, *germinal vesicle* and *germinal spot* respectively. The attraction sphere is not shown in the diagram.

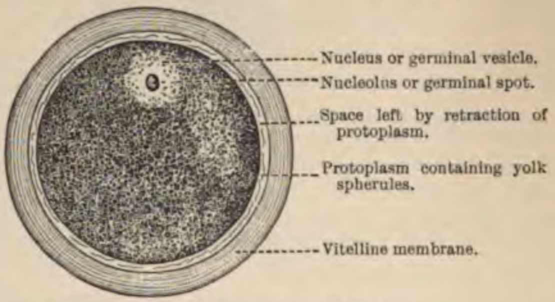

Nucleus or germinal vesicle.
Nucleolus or germinal spot.
Space left by retraction of protoplasm.
Protoplasm containing yolk spherules.
Vitelline membrane.

FIG. 26.—Representation of a human ovum. (Cadiat.)

The formation of ova will form the subject of a chapter later on, but it is convenient here at the outset to state briefly one or two facts, and introduce to the student a few terms which we shall have to employ frequently in the intervening chapters.

The ovum first discharges from its interior a portion of its nucleus, which forms two little globules upon it called the polar globules.

Fertilisation then occurs; that is to say, the head or nucleus of a male cell called a spermatozoon penetrates into the ovum, and becomes fused with the remains of the female nucleus.

Cell division or segmentation then begins, and the early stages are represented in the next figure.

Fluid discharged from the cells accumulates within the interior of the mulberry mass seen in fig. 27 *d*, and later, if a section is cut through it, the cells will be found arranged in three layers.

The outermost layer is called the **epiblast.**

The middle layer is called the **mesoblast.**

The innermost layer is called the **hypoblast.**

From these three layers the growth of the rest of the body occurs, nutritive material being derived from the mother in mammals by means of an organ called the placenta.

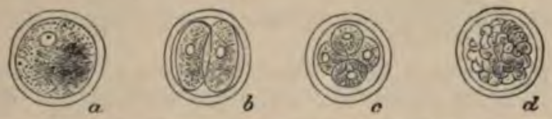


FIG. 27.—Diagram of an ovum (*a*) undergoing segmentation. In (*b*) it has divided into two, in (*c*) into four; and in (*d*) the process has resulted in the production of the so-called "mulberry-mass." (Frey.)

The *epiblast*, the outermost layer of the embryo, forms the epidermis, the outermost layer of the adult. It also forms the nervous system.

The *hypoblast*, the innermost layer of the embryo, forms the lining epithelium of the alimentary (except that of the mouth and anus which are involutions from the epiblast) and respiratory tracts, that is, the innermost layer of the adult. It also forms the cellular elements in the large digestive glands, such as the liver and pancreas, which are originally, like the lungs, outgrowths from the primitive digestive tube.

The *mesoblast* forms the remainder, that is, the great bulk of the body, including the muscular, osseous, and other connective tissues; the circulatory and urino-genital systems.

CHAPTER III

EPITHELIUM

THE elementary tissues of which the organs of the body are built up may be arranged into four groups: epithelial, connective, muscular, and nervous. The first of these, the epithelial tissues, follows naturally on a study of the animal cell, as an epithelium may be defined as a tissue composed entirely of cells united by a minimal amount of cementing material. As a rule, an epithelium is spread out as a membrane covering a surface or lining the cavity of a hollow organ.

These epithelia may be grouped into two great classes, each of which may be again subdivided according to the shape and arrangement of the cells of which it is composed. The following table gives the principal varieties:—

CLASS 1.—*Simple epithelium;* that is, an epithelium consisting of one layer of cells only. Its subgroups are as follows:—

- *a.* Pavement epithelium.
- *b.* Cubical and columnar epithelium.
- *c.* Ciliated epithelium.

CLASS 2.—*Compound epithelium;* that is, an epithelium consisting of more than one layer of cells. Its subgroups are as follows:—

- *a.* Transitional epithelium.
- *b.* Stratified epithelium.

This classification does not include the more specialised forms of epithelium found in secreting glands, or in the sense organs, nor structures like hair, and enamel of tooth, which are epithelial in origin. These will be considered in their proper place later on.

Pavement Epithelium.

This consists of a layer of thin cells, arranged like flat pavement-stones accurately fitting together and united by a small amount of cementing material. The structure of the cells and their outlines may be best demonstrated in the following way:—

A portion of the fresh tissue is taken and immersed for a few minutes in a 1 per cent. solution of nitrate of silver; it is taken out, washed with distilled water, and exposed in water or spirit to sunlight. The silver forms a compound with the cement, which in the light is decomposed or reduced, leading to a fine deposit of silver, showing as black or brown lines between the cells, and accurately defining their outlines. The preparation may then be immersed in some stain like logwood to bring out the nuclei, and finally mounted in the usual way.

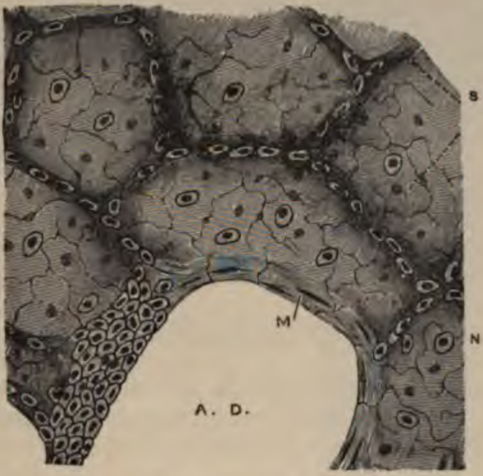


FIG. 28.—From a section of the lung of a cat, stained with silver nitrate. N. Alveoli or air-cells, lined with large flat, nucleated cells, with some smaller polyhedral nucleated cells. (Klein and Noble Smith.)

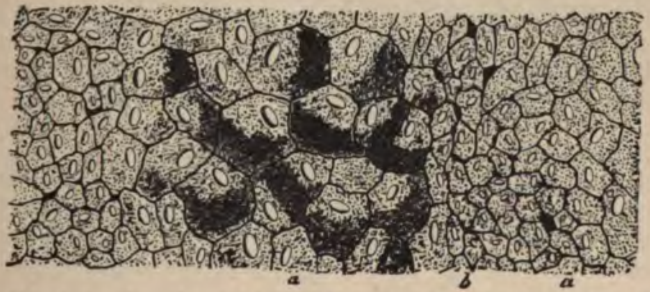


FIG. 29.—Abdominal surface of central tendon of the diaphragm of rabbit, showing the general polygonal shape of the endothelial cells; each cell is nucleated. × 300. (Klein.)

Fig. 28 shows the appearance presented in a preparation of lung. In the alveoli or air-sacs of the lung, pavement epithelium of a typical kind is found forming a lining membrane.

Endothelium.—Epithelium of similar appearance is found lining the interior of the whole of the vascular system, heart, arteries, capillaries, veins, and lymphatics, and in the adjuncts of the circulatory system called the serous membranes (pericardium, peritoneum, etc.).

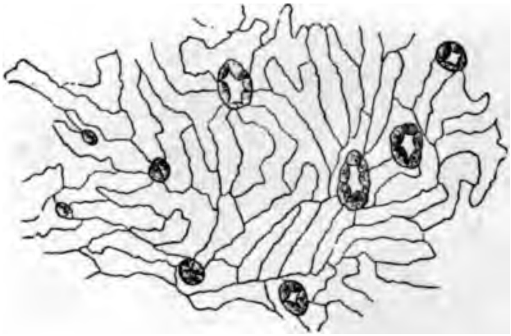


FIG. 30.—Peritoneal surface of a portion of the septum of the great lymph-sac of a frog. The stomata, some of which are open, some collapsed, are well shown. × 160. (Klein.)

This epithelium is formed from the middle layer of the embryo, the mesoblast; most other epithelium is derived either from epiblast or hypoblast. Hence it has received a distinct name, viz.: *endothelium.*

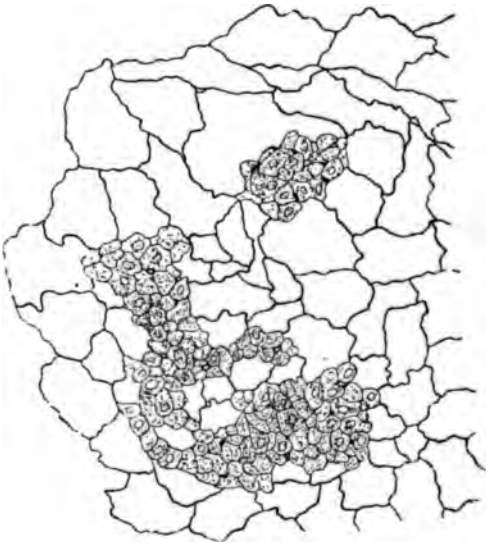


FIG. 31.—A portion of the great omentum of dog, which shows, amongst the flat endothelium of the surface, small and large groups of germinating endothelium, between which are many stomata. × 300. (Klein.)

The general appearance presented by endothelium in serous membranes is shown in figs. 29, 30, and 31; in blood-vessels in fig. 32.

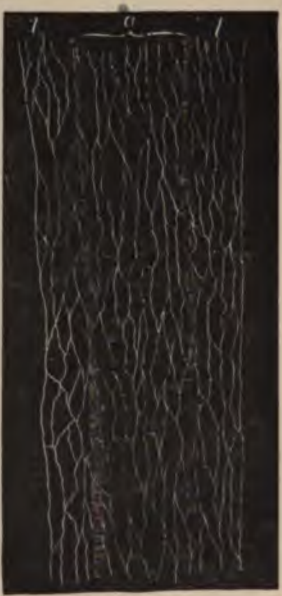


FIG. 32.—Surface view of an artery from the mesentery of a frog, ensheathed in a peri-vascular lymphatic vessel. *a*, The artery, with its circular muscular coat (media) indicated by broad transverse markings, with an indication of the adventitia outside. *l*, Lymphatic vessel; its wall is a simple endothelial membrane. (Klein and Noble Smith.)

The stomata seen in some of the drawings are minute openings surrounded by more darkly staining cells, which lead from serous cavities into lymphatic vessels.

Cubical, Spheroidal, and Columnar Epithelium.

In these forms of epithelium, the cells are not flat, but are thick; if they approximate cubes or spheres in shape, the epithelium is called cubical or spheroidal respectively. *Polyhedral* epithelium is found in the alveoli of secreting glands, such as the salivary glands, liver, and pancreas (see figs. 33 and 34), and will be discussed at length in connection with those organs. *Cubical* epithelium is found in the alveoli of the thyroid (see fig. 35), in the tubules of the testis, and in the ducts of some glands.

In *columnar* epithelium the cells are tall, and form a kind of palisade or rows of columns. It is found lining the interior of the stomach and intestines, and the ducts of the majority of secreting glands; it forms also the layer on the outer surface of the ovary.

In the intestinal epithelium each cell has a distinct brightly refracting and striated border. Fig. 36 shows two isolated cells of this kind.

The nucleus with its usual network and the vacuolated condition of the protoplasm are very well seen. The attached border is narrower than the free edge. Amœboid lymph cells are found in the spaces that must necessarily be left when cells of such a shape cover a surface. Fig. 37 shows a row of columnar cells from the rabbit's intestine.

The next figure (fig. 38) shows the arrangement of these cells on the surface of a villus, one of the numerous little projections found in the small intestine.

The gaps seen there are due to the formation of what are called goblet cells. In some of the columnar cells, a formation of granules occurs which consist of a substance called mucigen; these run together, and are discharged from the cell as a brightly refracting globule of mucin, leaving the cell with open mouth like a goblet, the nucleus being surrounded by the remains of the protoplasm in its narrow stem (see fig. 39).

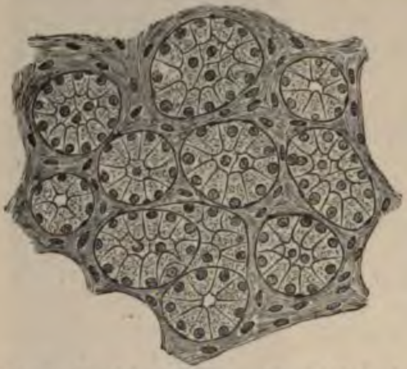


FIG. 33.—Glandular epithelium. Small lobule of a mucous gland of the tongue, showing nucleated glandular cells. × 200. (V. D. Harris.)

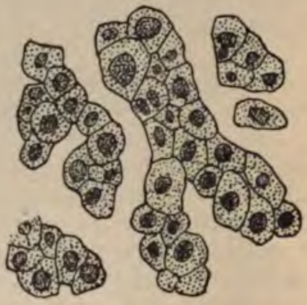


FIG. 34.—A small piece of the liver of the horse. (Cadiat.)

This transformation is a normal process continually going on throughout life, the discharged *mucin* contributing to form *mucus.* The cells themselves may recover their original shape after discharge, and repeat the process later on.

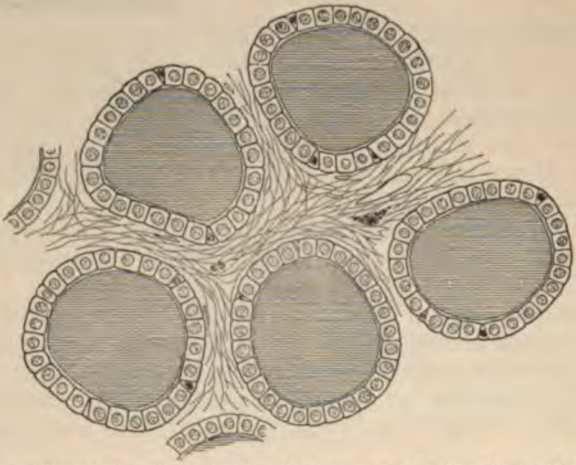


FIG. 35.—Section of human thyroid; the few vesicles shown are lined by cubical epithelium, and contain a colloid material. (After Schäfer.)

Ciliated Epithelium.

The cells of ciliated epithelium are generally of columnar shape (fig. 40), but they may occasionally be spheroidal (fig. 41).

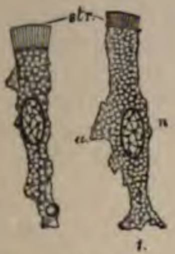


FIG. 36.—Columnar epithelium cells of the rabbit's intestine. The cells have been isolated after maceration in very weak chromic acid. The cells are much vacuolated, and one of them has a fat globule near its attached end. The striated border (*str.*) is well seen, and the bright disc separating it from the cell protoplasm. *n*, nucleus with intranuclear network. *a*, a thinned-out winglike projection of the cell which probably fitted between two adjacent cells. (Schäfer.)

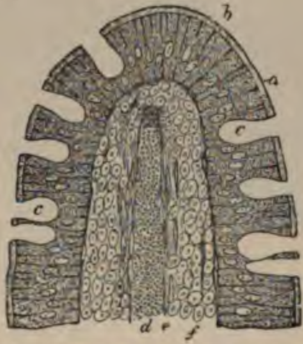


FIG. 38.—Vertical section of an intestinal villus of a cat. *a*, the striated border of the epithelium; *b*, columnar epithelium; *c*, goblet cells; *d*, central lymph-vessel; *e*, unstriped muscular fibres; *f*, adenoid stroma of the villus in which are contained lymph-corpuscles. (Klein.)

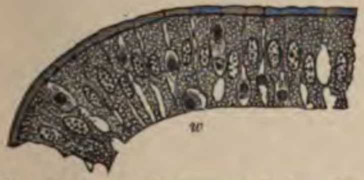


FIG. 37.—A row of columnar cells from the rabbit's intestine. Smaller cells are seen between the epithelium cells; these are lymph-corpuscles. (Schäfer.)

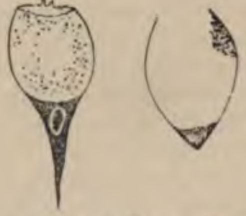


FIG. 39.—Goblet cells. (Klein.)

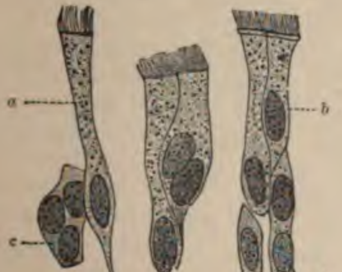


FIG. 40.—Ciliated epithelium from the human trachea. *a*, large fully-formed cell; *b*, shorter cell; *c*, developing cells with more than one nucleus. (Cadiat.)

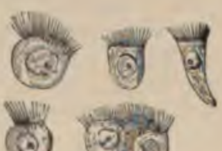


FIG. 41.—Spheroidal ciliated cells from the mouth of the frog. × 300 diameters. (Sharpey.)

Each cell is surmounted by a bunch of fine tapering filaments. They were originally called *cilia* because of their resemblance in shape to eyelashes. They differ from eyelashes in being extremely small, and in not being stiff; they are in fact composed of protoplasm. During life these move to and fro, and so produce a current of fluid over the surface they cover. Like columnar cells, they may form goblet cells and discharge mucin.

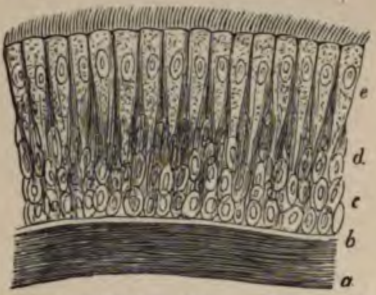


FIG. 42.—Ciliated epithelium of the human trachea. *a*, layer of longitudinally arranged elastic fibres; *b*, basement membrane; *c*, deepest cells, circular in form; *d*, intermediate elongated cells; *e*, outermost layer of cells fully developed and bearing cilia. × 350. (Kölliker.)

In the larger ciliated cells, it will be seen that the border on which the cilia are set is bright, and composed of little knobs, to each of which a cilium is attached; in some cases the knobs are prolonged into the cell protoplasm as filaments or rootlets (fig. 43). According to some observers these rootlets are outgrowths from the multiplied centrosome of the cell.

The bunch of cilia is homologous with the striated border of columnar cells.

Ciliated epithelium is found in the human body, (1) lining the air passages, but not in the alveoli of the lungs; these are lined by pavement epithelium; (2) in the Fallopian tubes and upper part of the uterus; (3) in the ducts of the testis known as the vasa efferentia and coni vasculosi; here the cilia are the longest found in the body; (4) in the ventricles of the brain and central canal of the spinal cord; (5) the tail of a spermatozoon may also be regarded as a long cilium.

In other animals cilia are found in other parts; for instance, in the frog the mouth and gullet are lined by ciliated cells; in the tadpole, the whole surface of the body and especially the gills are covered with cilia. Among the invertebrates one finds many protozoa completely covered with cilia; in many embryos the cilia are arranged in definite bands round the body; in the rotifers or wheel animalcules, a ring of cilia round the mouth gives the name to this par-

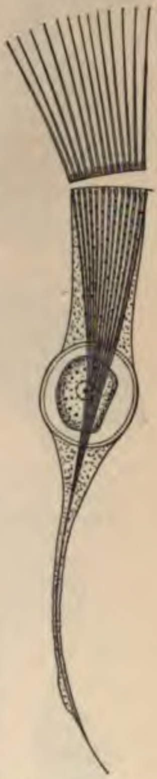


FIG. 43.—Ciliated cell from the intestine of a mollusc. (Engelmann.)

ticular group. The gills of many animals are covered with cilia; and the cells of the kidney tubules in some animals are ciliated.

Ciliary Motion.

Ciliary motion reminds one of amœboid movement, but it is much more rapid, and more orderly. It consists of a rhythmical movement of the cilia, a bending over, followed by a lessening of the curvature, repeated with great frequency.

When living ciliated epithelium, *e.g.*, from the gill of a mussel, or from the mouth of the frog, is examined under the microscope in a drop of 0·75 per cent. solution of common salt (*normal saline solution*), the cilia are seen to be in constant rapid motion, each cilium being fixed at one end, and swinging or lashing to and fro. The general impression given to the eye of the observer is very similar to that produced by waves in a field of corn, or swiftly running and rippling water, and the result of their movement is to produce a continuous current in a definite direction, and this direction is the same on the same surface, being usually in the case of a cavity towards the external orifice.

There is not only rhythmicality in the movement of a single cilium, but each acts in harmony with its fellows in the same cell, and on neighbouring cells.

The uses of cilia can from the above be almost guessed; in the respiratory passages they create a current of mucus with entangled dust towards the throat; in the Fallopian tube or oviduct they assist the ovum on its way to the uterus; in the gullet of the frog they act downwards and assist swallowing; in the ciliated protozoa they are locomotive organs. Over the gills of marine animals they keep up a fresh supply of water, and in the case of the rotifers, which are fixed animals, the current of water brings food to the mouth.

Ciliary motion is independent of the will, and of the influence of the nervous system. It may continue for several hours after death or removal from the body, provided the portion of tissue under examination be kept moist. Its independence of the nervous system is shown also in its occurrence in the lowest invertebrate animals, which are unprovided with anything analogous to a nervous system. The vapour of ether or chloroform and carbon dioxide arrest the motion, but it is renewed on the discontinuance of the application. The movement ceases when the cilia are deprived of oxygen, although it may continue for a time in the absence of *free* oxygen, but is revived on the admission of this gas. The contact of various substances, *e.g.*, bile, strong acids, and alkalis, will stop the motion altogether; but this depends on destruction of the delicate substance of which the cilia are composed. Temperatures above 45° C. and near

0° C. stop the movement, whereas moderate heat and dilute alkalis are favourable to the action, and revive the movement after temporary cessation. The exact explanation of ciliary movement is not known; whatever may be the exact cause, the movement must depend upon some changes going on in the cell to which the cilia are attached, as when the latter are cut off from the cell the movement ceases, and when severed so that a portion of the cilia are left attached to the cell, the attached and not the severed portions continue the movement. It has been suggested by Engelmann that the contractile part of the protoplasm is only on the concave side of a curved cilium, and that when this contracts that the cilium is brought downwards; where relaxation occurs, the cilium rebounds by the elastic recoil of the convex border.

Schäfer has suggested that the flow of hyaloplasm backwards and forwards will explain ciliary as it will amœboid movement. In an amœboid cell, the spongioplasm is irregular in arrangement, hence an outflow of hyaloplasm from it can occur in any direction. But in the curved projection called a cilium, the hyaloplasm can obviously flow in only one direction into the cilium and back again. The flow of more hyaloplasm into the spongioplasm of the cilium will cause it to curve, the flow of the hyaloplasm back into the body of the cell will cause the cilium to straighten.

The action of dilute alkalis and acids on cilia is interesting. Dilute acids stop ciliary motion; and cilia, if allowed to act in salt solution for a time, get more and more languid, and finally cease acting; in popular language they become fatigued. Now we shall find in muscle that fatigue is largely due to the accumulation of the acid products of muscular activity; remove the sarco-lactic acid and fatigue passes off. It is probable that the same occurs in other contractile tissues; the cilia gradually stop, due to acid products of their activity collecting around them; when these are neutralised with dilute alkali the cilia resume activity.

Transitional Epithelium.

This term has been applied to cells which are neither arranged in a single layer, as is the case with simple epithelium, nor yet in many superimposed strata, as in stratified epithelium; in other words, it is employed when epithelial cells are found in two, three, or four superimposed layers.

The upper layer may be either columnar, ciliated, or squamous. When the upper layer is columnar or ciliated the second layer consists of smaller cells fitted into the inequalities of the cells above them, as in the trachea (fig. 42).

The epithelium which is met with lining the urinary bladder and ureters is, however, the transitional *par excellence.* In this variety there are two or three layers of cells, the upper being more or less flattened according to the full or collapsed condition of the organ, their under surface being marked with one or more depressions, into which the heads of the next layer of club-shaped cells fit. Between the lower and narrower parts of the second row of cells are fixed the irregular cells which constitute the third row; sometimes a fourth row is present (fig. 44). If a scraping of the mucous membrane of the bladder is teased, and examined under the microscope, all these forms may be made out (fig. 45). Each cell contains a large nucleus, and the larger and superficial cells often possess two.

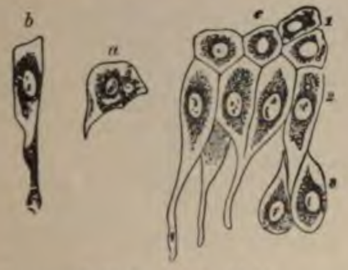


FIG. 44.—Epithelium of the bladder. *a*, one of the cells of the first row; *b*, a cell of the second row; *c*, cells *in situ*, of first, second, and deepest layers. (Obersteiner.)

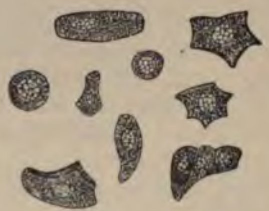


FIG. 45.—Transitional epithelial cells from a scraping of the mucous membrane of the bladder of the rabbit. (V. D. Harris.)

Stratified Epithelium.

The term *stratified epithelium* is employed when the cells forming the epithelium are arranged in a considerable number of superimposed layers. The shape and size of the cells of the different layers, as well as the number of the layers, vary in different situations; but the superficial cells are, as a rule, of the squamous, or scaly variety, and the deepest of the columnar form.

The cells of the intermediate layers are of different shapes, but those of the middle layers are more or less rounded. The superficial cells are broad and overlap by their edges (fig. 46). Their chemical composition is different from that of the underlying cells, as they contain keratin, and are therefore horny in character.

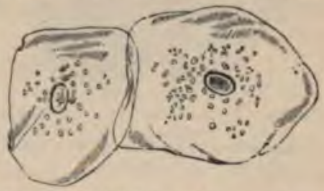


FIG. 46.—Epithelium scales from the inside of the mouth. × 260. (Henle.)

The really cellular nature of even the dry and shrivelled scales cast off from the surface of the epidermis can be proved by the application of caustic potash, which rapidly causes them to swell and assume their original form. Their nuclei, however, have disappeared.

The squamous cells exist in the greatest number of layers in the epidermis or superficial part of the skin; the most superficial of these are being continually removed by friction, and new cells from below supply the place of those cast off.

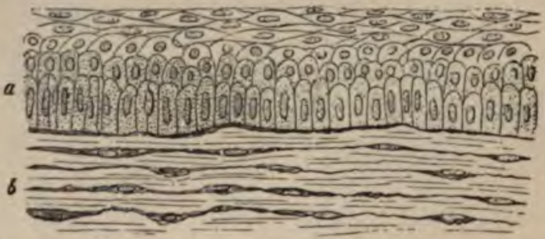


FIG. 47.—Vertical section of the stratified epithelium of the rabbit's cornea. *a*, anterior epithelium, showing the different shapes of the cells at various depths from the free surface; *b*, a portion of the substance of cornea. (Klein.)

In many of the deeper layers in the mouth and skin the outline of the cells is very irregular, in consequence of processes passing from cell to cell across these intervals.

Such cells (fig. 48) are termed "ridge and furrow," "cogged" or "prickle" cells. These "prickles" are prolongations of the intra-cellular network which run across from cell to cell, thus joining them together, the interstices being filled by lymph and transparent inter-cellular cement substance. When this increases in quantity in inflammation the cells are pushed further apart, and the connecting fibrils or "prickles" are elongated and therefore more clearly visible.

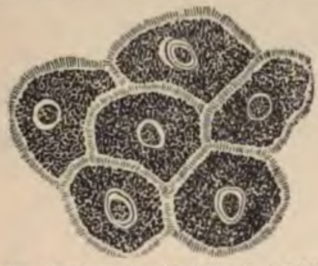


FIG. 48.—Jagged cells from the middle layers of stratified epithelium, from a vertical section of the gum of a new-born infant. (Klein.)

This connection of cell to cell is sometimes spoken of as *continuity of protoplasm*; the same occurs in involuntary muscular tissue. It is very marked in the tissues of many plants.

The columnar cells of the deepest layer are distinctly nucleated; they multiply rapidly by division; and as new cells are formed beneath, they press the older cells forwards to be in turn pressed forwards themselves towards the surface, gradually becoming flatter in shape and horny in composition until they are cast off from the surface.

Stratified epithelium is found in the following situations:—(1) Forming the epidermis, covering the whole of the external surface of the body; (2) Covering the mucous membrane of the nasal orifice, tongue, mouth, pharynx, and œsophagus; (3) As the conjunctival epithelium, covering the cornea; (4) Lining the vagina and the vaginal part of the cervix uteri.

Nutrition of Epithelium.

Epithelium has no blood-vessels; it is nourished by lymph. When the blood is circulating through the thin-walled small blood-vessels in the tissues beneath the epithelium, some of its fluid constituents escape. This fluid is called *lymph;* it penetrates to all parts of the cellular elements of tissues and nourishes them. In the thicker varieties of epithelium, the presence of the irregular minute channels between the prickle cells (fig. 48) enables the lymph to soak more readily between the cells than it would otherwise be able to do. Epithelium is also destitute of nerves as a rule. But in stratified epithelium, particularly that covering the cornea at the front of the eye and in the deeper layers of the epidermis, a plexus of nerve fibrils is found.

Chemistry of Epithelium.

There is not much to add to what has been already stated concerning cells; protoplasm and nucleus have the same chemical composition as has been already described in Chapter II. Two new substances have, however, been mentioned in the foregoing chapter—namely, mucin and keratin.

Mucin.—This is a widely distributed substance occurring in epithelial cells or shed out by them (see goblet cells, fig. 39). It also forms the chief constituent of the cementing substance between epithelial cells. We shall again meet with it in the intercellular substance of the connective tissues. The mucin obtained from different sources varies somewhat in composition and reactions, but they all agree in the following points:—

(a) Physical character: viscid and tenacious.

(b) Precipitability from solutions by acetic acid. They all dissolve in dilute alkalis, like lime-water.

(c) They are all compounds of proteid, with a carbohydrate material; by treatment with mineral acid this is hydrated into a reducing but non-fermentable sugar-like substance.

The substance mucin, when it is formed within cells (goblet cells, cells of mucous glands), is preceded in the cells by granules of a substance which is not mucin, but is readily changed into mucin. This precursor, or mother-substance of mucin, is called *mucigen* or *mucinogen.*

Keratin, or horny material, is the substance found in the surface layers of the epidermis, in hairs, nails, hoofs, and horns. It is very insoluble, and chiefly differs from proteids in its high percentage of sulphur. Keratin is a member of a heterogeneous group of proteid-like substances which are called albuminoids, and several more members of this group we shall have to consider in our next chapter on the connective tissues.

CHAPTER IV

THE CONNECTIVE TISSUES

THE connective tissues are the following:—

1. Areolar tissue.
2. Fibrous tissue.
3. Elastic tissue.
4. Adipose tissue.
5. Retiform and lymphoid tissues.
6. Jelly-like tissue.
7. Cartilage.
8. Bone and dentine.
9. Blood.

At first sight these numerous tissues appear to form a very heterogeneous group, including the most solid tissues of the body (bone, dentine) and the most fluid (blood).

But on examining a little more deeply, one finds that the grouping of these apparently different tissues together depends on a number of valid reasons, which may be briefly stated as follows:—

1. They all resemble each other in origin. All are formed from the mesoblast, the middle layer of the embryo.
2. They resemble each other structurally; that is to say, the cellular element is at a minimum, and the intercellular material at a maximum.
3. They resemble each other functionally; they form the skeleton, and act as binding, supporting, or connecting tissues to the softer and more vital tissues.

An apology is sometimes made for calling the blood a tissue, because one's preconceived idea of a tissue or texture is that it must be something of a solid nature. But all the tissues contain water. Muscular tissue contains, for instance, at least three-quarters of its weight as water. Blood, after all, is not much more liquid than muscle. Blood, moreover, contains cellular elements analogous to the cells of other tissues, but separated by large quantities of a fluid intercellular material called blood-plasma.

Blood is also mesoblastic, and thus the two first characteristics of a connective tissue are present. It does not fulfil the third condition by contributing to the support of the body as part of the skeleton, but it does so in another sense, and serves to support the body by conveying nutriment to all parts.

Areolar Tissue.

This is a very typical connective tissue. It has a wide distribution, and constitutes the subcutaneous, subserous, and submucous tissues. It forms sheaths (fasciæ) for muscles, nerves, blood-vessels, glands, and internal organs, binding them in position and penetrating into their interior, supports and connects their individual parts.

If one takes a little of the subcutaneous tissue from an animal, and stretches it out on a glass slide, it appears to the naked eye like a soft, fleecy network of fine white fibres, with here and there wider fibres joining it. It is, moreover, elastic.

But in order to make out its structure accurately, it is necessary to examine the thinnest portions of the film with the microscope, and the action of staining and other reagents may then be also studied. By such means it is seen that this typical connective tissue consists of four different kinds of material, or, as they may be termed, *histological elements.* They are:—

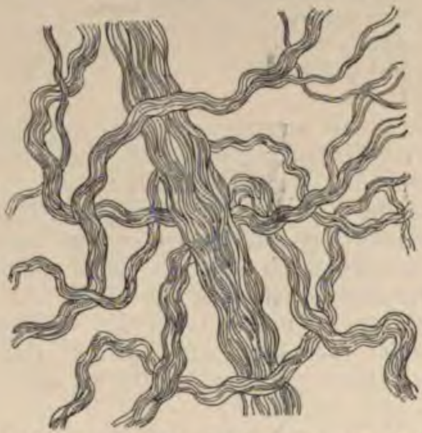


FIG. 49.—Bundles of the white fibres of areolar tissue partly unravelled. (After Sharpey.

(a) Cells, or connective-tissue corpuscles.
(b) A homogeneous matrix, ground substance, or intercellular material.
(c) White fibres } These are deposited in the matrix.
(d) Yellow or elastic fibres }

In considering these four histological elements we may first take the fibres, because they are the most obvious and abundant of the structures observable.

The white fibres. These are exquisitely fine fibres collected into bundles which have a wavy outline. The bundles run in different directions, forming an irregular network, the meshes between which are called *areolæ;* hence the name areolar. The individual fibres never branch or join other fibres, but they may pass from one bundle to another.

On treatment with dilute acetic acid they become swollen and indistinct, leaving the other structures mixed with them more apparent.

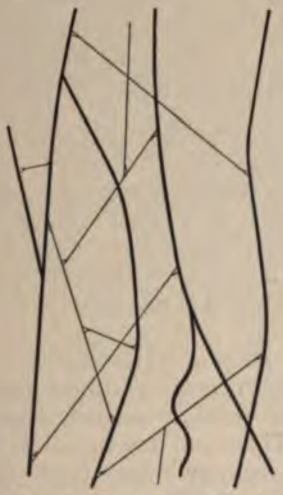


Fig. 50.—Elastic fibres of areolar tissue. (After Schäfer.)

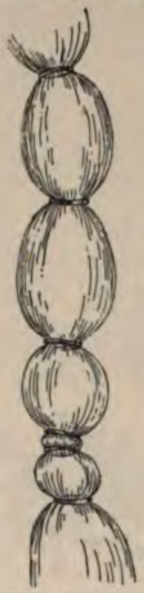


Fig. 51.—A white bundle swollen by acetic acid. (Toldt.)

They are composed of the chemical substance called *collagen.* On boiling they yield *gelatin;* some chemists regard collagen as the anhydride of gelatin; but whether this is so or not, the gelatin is undoubtedly derived from the collagen. Gelatin is a proteid-like substance though not a proteid. It belongs to the class of albuminoids. Its most characteristic property is its power of jellying or gelatinising; that is, it is soluble in hot water, but on cooling the solution it sets into a jelly.

The yellow or elastic fibres. These are seen readily after the white fibres are rendered almost invisible by treatment with dilute acetic acid, or after staining with such dyes as magenta and orcein, for which elastic fibres have a great affinity. They are bigger than the white fibres, have a distinct outline, and a straight course; they run singly, branch, and join neighbouring fibres (fig. 50).

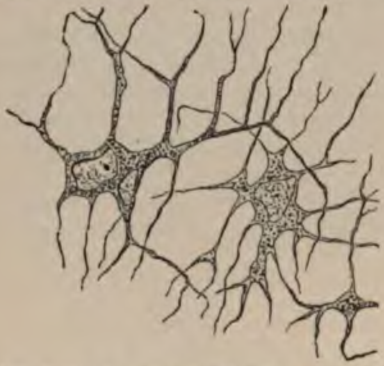


FIG. 52.—Horizontal preparation of the cornea of frog, stained with gold chloride; showing the network of branched corneal corpuscles. The ground substance is completely colourless. × 400. (Klein.)

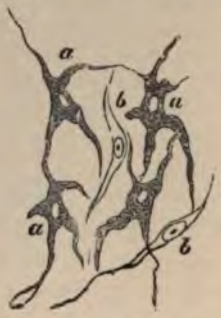


FIG. 53.—Ramified pigment-cells, from the tissue of the choroid coat of the eye. × 350. a, Cell with pigment; b, colourless fusiform cells. (Kölliker.)

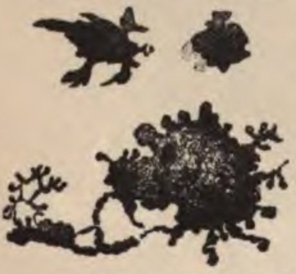


FIG. 54.—Flat, pigmented, branched connective-tissue cells from the sheath of a large blood-vessel of the frog's mesentery; the pigment is not distributed uniformly throughout the substance of the larger cell, consequently some parts of it look blacker than others (uncontracted state). In the two smaller cells most of the pigment is withdrawn into the cell-body, so that they appear smaller, blacker, and less branched. × 350. (Klein and Noble Smith.)

The material of which the elastic fibres are composed is called *elastin;* this is another albuminoid. It is unaltered, as we have seen, by dilute acid. It also resists the action of very strong acid, and is not affected by boiling water.

The bundles of white fibres which have been swollen out by dilute acetic acid sometimes exhibit constrictions as in fig. 51. These are due to elastic fibres or cell processes encircling them and preventing the swelling at those points.

Connective-tissue corpuscles. These are the cells of connective tissue: several varieties may be made out, especially after a preparation has been stained.

1. Flattened cells, branched, and often united by their processes, as in the cornea.
2. Flattened cells, unbranched, and joined edge to edge like the cells of an epithelium; these are well seen in the sheath of a tendon.
3. Plasma cells of Waldeyer, varying greatly in size and form, but not flattened. The protoplasm is much vacuolated.

4. Granule cells ("mast" cells of Ehrlich): like plasma cells, but containing albuminous granules (stainable by basic aniline dyes) instead of vacuoles.
5. Wander cells: white blood-corpuscles which have emigrated from the neighbouring blood-vessels.
6. Pigment cells: these are seen in the subcutaneous tissues of many animals, *e.g.*, the frog, and in the choroid coat of the eyeball.

Fig. 55 shows a highly magnified view of a small piece of subcutaneous tissue, and illustrates the irregular way in which the fibres and cells are intermixed.

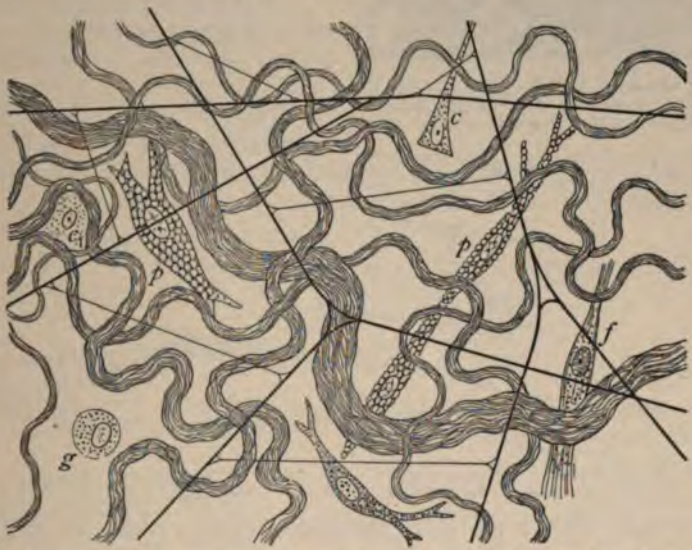


FIG. 55.—Areolar tissue. The white fibres are seen in wavy bundles; the elastic fibres form an open network. *p*, *p*, Plasma cells; *g*, granule cell; *c*, *c*, lamellar cells; *f*, fibrillated cell. (After Schäfer.)

The ground-substance. This may be represented in fig. 55 by the white background of the paper.

It may be readily demonstrated in a silver nitrate preparation; for the intercellular material has the same property of reducing silver salts in the sunlight that the cement-material of epithelium has. It becomes in consequence dark brown, with the exception of the spaces occupied by the corpuscles.

The spaces intercommunicate like the cells, and being considerably larger than the cells form a ramifying network of irregular channels, which were first termed by v. Recklinghausen the *Saft Kanälchen*, or little juice canals. Areolar tissue is certainly provided with blood-vessels, but the tissue elements are, as in all tissues, provided with nutriment by the exudation from the blood called *lymph*. The *Saft Kanälchen* enable the lymph to penetrate to every part of the areolar tissue.

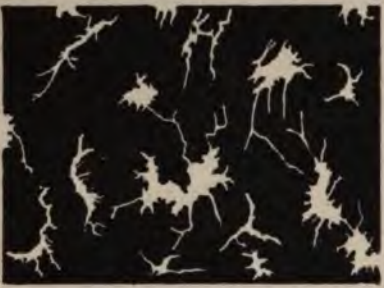


FIG. 56.—Ground-substance of connective tissue, stained by silver nitrate. The cell spaces are left white. (After Schäfer.)

Development of Areolar Tissue.

The mesoblastic cells in those parts where the tissue is to be formed become branched and fusiform.

These ultimately become the connective-tissue corpuscles, and they get more and more widely separated by intercellular material, partly shed out by the cells themselves, partly shed out from the neighbouring blood-vessels. This becomes the ground-substance.

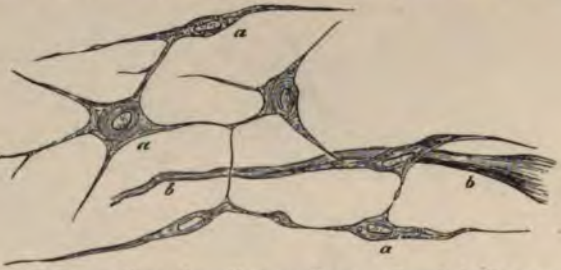


FIG. 57.—Portion of submucous tissue of gravid uterus of sow. *a*, Branched cells, more or less spindle-shaped; *b*, bundles of connective tissue. (Klein.)

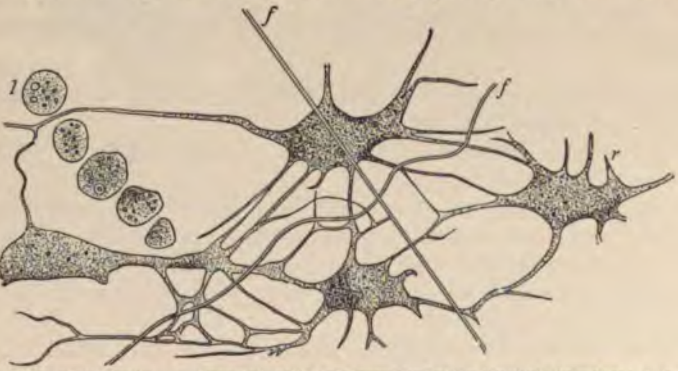


FIG. 58.—Jelly of Wharton. *r*, Ramified cells intercommunicating by their branches; *l*, a row of lymph-cells; *f*, fibres developing in the ground-substance. (Ranvier.)

The fibres are subsequently deposited in this matrix. At one time it was believed that the cells themselves became elongated and converted into fibres. No doubt the cells do exercise a controlling influence on fibre-formation in their neighbourhood, but it is certain that they never become fibres. The formation of fibres is intercellular. Some of the fibres formed are of the white, others of the yellow variety. In the case of the elastic fibres, rows of granules of elastin are first deposited; these joining together in single or multiple rows form the long fibres: traces of this are seen in transverse markings occasionally noticeable in the larger elastic fibres.

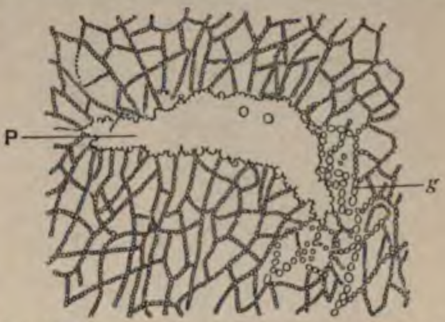


FIG. 59.—Development of elastic tissue by deposition of fine granules. *g*, Fibres being formed by rows of elastic granules; P, platelike expansion of elastic substance formed by the fusion of elastic granules. (Ranvier.)

Fibrous Tissue.

This is a kind of connective tissue in which the white fibres predominate; it is found in tendons and ligaments, in the periosteum, dura mater, true skin, the sclerotic coat of the eye, and in the thicker fasciæ and aponeuroses of muscle.

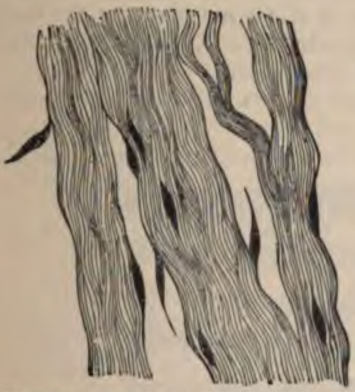


FIG. 60.—Fibrous tissue of tendon, consisting mainly of white fibres. (Stricker.)

The tissue is one of great strength; this is conferred upon it by the arrangement of the fibres, the bundles of which run parallel, union here, as elsewhere, giving strength. The fibres of the same bundle now and then intersect each other. The cells in tendons (fig. 61) are forced to take up a similar orderly arrangement, and are arranged in long chains in the ground-substance separating the bundles of fibres, and are more or less regularly quadrilateral with large round nuclei containing nucleoli, which are generally placed so as to be nearly contiguous in two cells. Each of these cells consists of a thick body, from which processes pass in various directions into, and partially fill up the spaces between, the bundles of fibres. The cells are generally marked by one or more lines or stripes when viewed longitudinally.

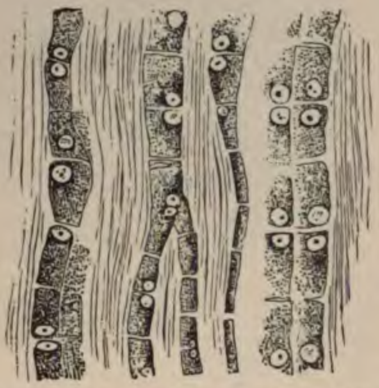


FIG. 61.—Caudal tendon of young rat, showing the arrangement, form, and structure of the tendon cells. The bundles of white fibres between which they lie have been rendered transparent and indistinct by the application of acetic acid. × 300. (Klein.)

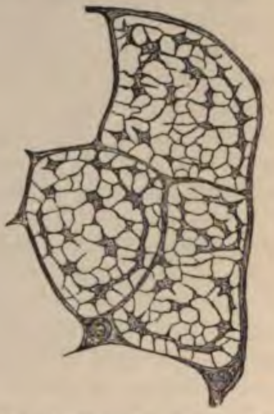


FIG. 62.—Transverse section of tendon from a cross section of the tail of a rabbit, showing sheath, fibrous septa, and branched tendon cells. The spaces left white in the drawing represent the tendinous bundles in transverse section. × 250. (Klein.)

This appearance is really produced by the wing-like processes of the cell, which project away from the chief part of the cell in different directions. These processes not being in the same plane as the body of the cell are out of focus, and give rise to these bright stripes when the cells are looked at from above and are in focus.

The branched character of the cells is seen in transverse section in fig. 62.

The cell spaces in which the cells lie are in arrangement like the cells; they can be brought into relief by staining with silver nitrate (see fig. 63).

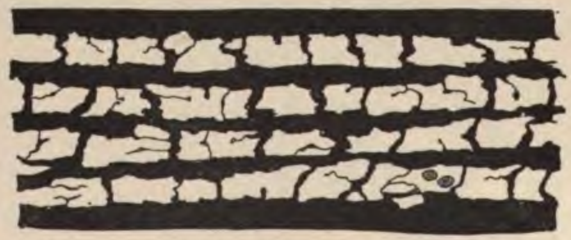


FIG. 63.—Cell spaces of tendon, brought into view by treatment with silver nitrate. (After Schäfer.)

Elastic Tissue.

This is a form of connective tissue in which the yellow or elastic fibres predominate. The yellow fibres are larger than those found in areolar tissue (see fig. 64), and are bound into bundles by areolar tissue. It is found in the ligamentum nuchæ of the ox, horse, and many other animals; in the ligamenta subflava of man; in the arteries and veins, constituting the fenestrated coat of Henle; in the lungs and trachea; in the stylo-hyoid, thyro-hyoid, and crico-thyroid ligaments; and in the true vocal cords.

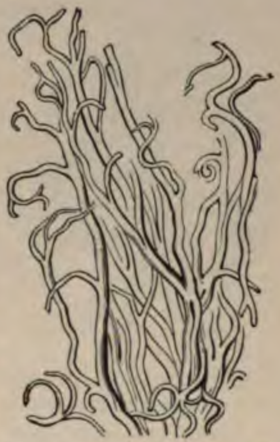


FIG. 64.—Elastic fibres from the ligamenta subflava. × 200. (Sharpey.)

Elastic tissue occurs in various forms, from a structureless, elastic membrane to a tissue whose chief constituents are bundles of fibres crossing each other at different angles; when seen in bundles elastic fibres are yellowish in colour, but individual fibres are not so distinctly coloured. The larger elastic fibres are often transversely marked, indicating their mode of origin (see p. 41), and on transverse section are seen to be angular (fig. 65).

Elastic tissue, being extensible and elastic (*i.e.*, recoiling after it has been stretched), has a most important use in assisting muscular tissue in a mechanical way, and so lessening the wear and tear of such an important tissue as muscle. Thus, in the ligamenta subflava of the human vertebral column it assists in the maintenance of the erect posture; in the ligamentum nuchæ in the neck of quadrupeds it assists in the raising of the head and in keeping it in that position. In the arterial walls, and in the air tubes and lungs, it has a similar important action, as we shall see when discussing the subjects of the circulation and respiration.

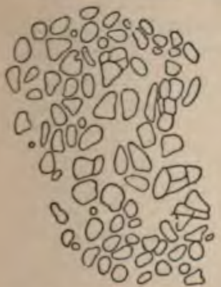


FIG. 65.—Transverse section of a portion of lig. nuchæ, showing the outline of the fibres. (After Stöhr.)

We now come to those forms of connective tissue in which the cells rather than the fibres are most prominent.

Adipose Tissue.

In almost all regions of the human body a larger or smaller quantity of adipose or fatty tissue is present; the chief exceptions being the subcutaneous tissue of the eyelids, penis and scrotum, the nymphæ, and the cavity of the cranium.

Adipose tissue is developed in connection with areolar tissue, and forms in its meshes little masses of unequal size and irregular shape, to which the term *lobules* is applied.

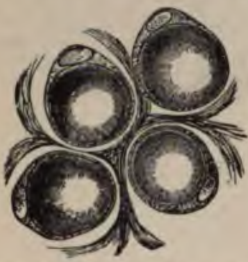


FIG. 66.—Fat-cells from the omentum of a rat. (Klein.)

Under the microscope adipose tissue is found to consist essentially of little vesicles or cells which present dark, sharply-defined edges when viewed with transmitted light: they are about $\frac{1}{400}$ or $\frac{1}{500}$ of an inch in diameter; each consists of a structureless and colourless membrane or bag formed of the remains of the original protoplasm of the cell, filled with fatty matter, which is liquid during life, but is in part solidified (or sometimes crystallised) after death. A nucleus is always present in some part or other of the cell protoplasm, but in the ordinary condition of the cell it is not easily or always visible (fig. 67).

This membrane and the nucleus can generally be brought into view by staining the tissue: it can be still more satisfactorily demonstrated by extracting the contents of the fat-cells with ether, when the shrunken, shrivelled membranes remain behind. By mutual pressure, fat-cells assume a polyhedral figure (fig. 68, *b*). When stained with osmic acid fat-cells appear black.

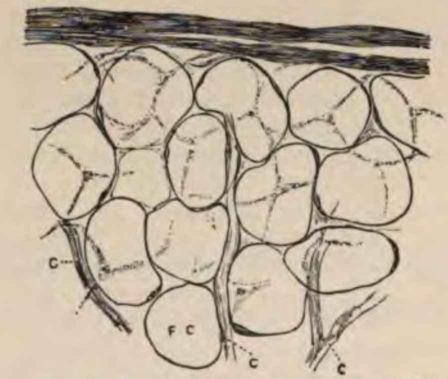


FIG. 67.—Group of fat-cells (F C) with capillary vessels (C). (Noble Smith.)

The oily matter contained in the cells is composed of the compounds of fatty acids with glycerin, which are named *olein*, *stearin*, and *palmitin*.

Development of Adipose Tissue.—Fat-cells are developed from connective-tissue corpuscles, especially the "mast"-cells; these cells may be found exhibiting every intermediate gradation between an ordinary granular corpuscle and a mature fat-cell. The process of development is as follows: a few small drops of oil make their appearance in the protoplasm, and by their confluence a larger drop is produced (figs. 69 and 70): this gradually increases in size at the expense of the original protoplasm of the cell, which becomes cor-

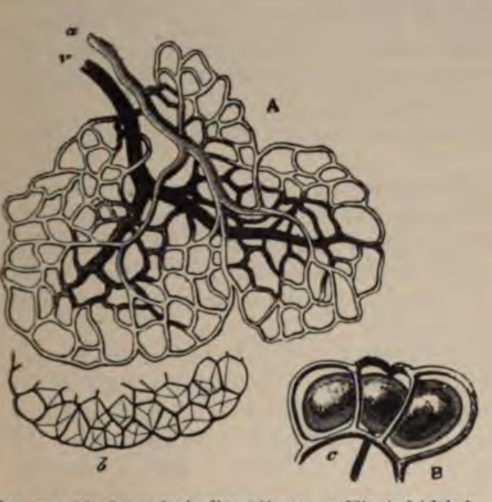


FIG. 68.—Blood-vessels of adipose tissue. A, Minute fat-lobule, in which the vessels only are represented. *a*, artery; *v*, vein; *b*, the fat-vesicles of one border of the lobule separately represented. × 100. B, Plan of the arrangement of the capillaries (*c*) on the exterior of the vesicles; more highly magnified. (Todd and Bowman.)

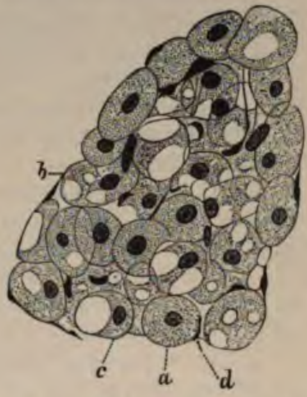


FIG. 69.—A lobule of developing adipose tissue from an eight months' fœtus. *a*, Spherical or, from pressure, polyhedral cells with large central nucleus, surrounded by protoplasm staining uniformly with hæmatoxylin. *b*, Similar cells with spaces from which the fat has been removed by oil of cloves. *c*, Similar cells showing how the nucleus with enclosing protoplasm is being pressed towards periphery. *d*, Nucleus of endothelium of investing capillaries. (M'Carthy.) Drawn by Treves.

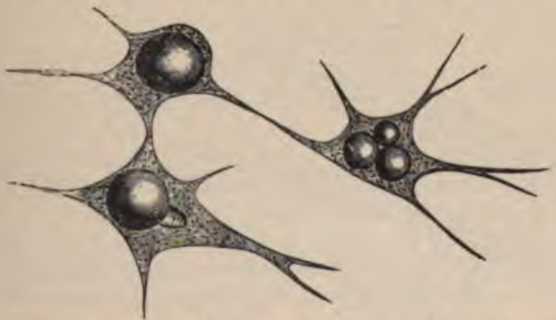


FIG. 70.—Branched connective-tissue corpuscles, developing into fat-cells. (Klein.)

respondingly diminished in quantity till in the mature cell it only forms a thin film, with a flattened nucleus imbedded in its substance (fig. 66).

Vessels and Nerves.—A large number of blood-vessels are found in adipose tissue, which subdivide until each lobule of fat contains a fine meshwork of capillaries ensheathing each individual fat-cell (fig. 68). Although nerve fibres pass through the tissue, no nerves have been demonstrated to terminate in it.

The Uses of Adipose Tissue.—Among the uses of adipose tissue these are the chief:—

a. It serves as a store of combustible matter which may be reabsorbed into the blood when occasion requires, and, being used up in the metabolism of the tissues, helps to preserve the heat of the body.

b. The fat which is situated beneath the skin must, by its want of conducting power, assist in preventing undue waste of the heat of the body by escape from the surface.

c. As a packing material, fat serves very admirably to fill up spaces, to form a soft and yielding yet elastic material wherewith to wrap tender and delicate structures, or form a bed with like qualities on which such structures may lie, not endangered by pressure. As examples of situations in which fat serves such purposes may be mentioned the palms of the hands, the soles of the feet, and the orbits.

d. In the long bones fatty tissue, in the form known as yellow marrow, fills the medullary canal, and supports the small blood-vessels which are distributed from it to the inner part of the substance of the bone.

Retiform Tissue.

Retiform or reticular tissue is a kind of connective tissue in which the ground substance is of more fluid consistency than elsewhere.

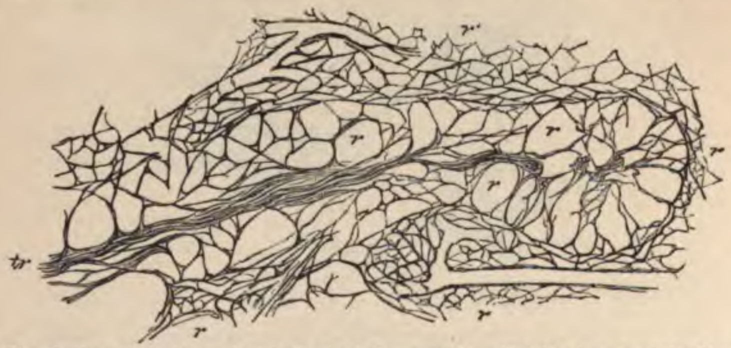


FIG. 71.—Retiform tissue from a lymphatic gland, from a section which has been treated with dilute potash. (Schäfer.)

There are few or no elastic fibres in it, but the white fibres run in very fine bundles forming a close network. The bundles are covered and concealed by flattened connective-tissue corpuscles. When these are dissolved by dilute potash, the fibres are plainly seen (fig. 71).

The statement has been made that the fibres of retiform tissue are chemically different from those of areolar tissue, in spite of the fact that they are indistinguishable microscopically, and in many places continuous with each other. Miss Tebb has conclusively proved that chemical differences do not exist between the two groups of fibres; both are made of collagen, and the substance termed reticulin by Siegfried is an artifact; it is merely collagen which has been rendered resistant and insoluble by the reagents (alcohol, ether) used in its preparation.

Adenoid or Lymphoid Tissue.

This is retiform tissue in which the meshes of the network are largely occupied by lymph corpuscles. These are in certain foci actively multiplying; they get into the lymph stream, which washes them into the blood, where they become the colourless corpuscles. It is found in the lymphatic glands, the thymus, the tonsils, in the follicular glands of the tongue, in Peyer's patches, and in the solitary glands of the intestines, in the Malpighian corpuscles of the spleen, and under the epithelium of many mucous membranes.

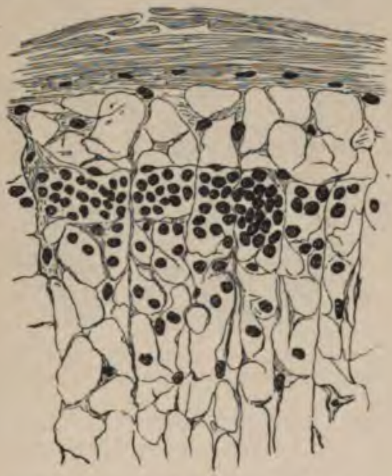


FIG. 72.—Part of a section of a lymphatic gland, from which the corpuscles have been for the most part removed, showing the supporting retiform tissue. (Klein and Noble Smith.)

Basement Membranes.

These are homogeneous in appearance, and are found between the epithelium of a mucous membrane and the subjacent connective tissue. They are generally formed of flattened connective-tissue corpuscles joined together by their edges, but sometimes they are made of condensed ground-substance, not of cells, and in other cases again (as in the cornea) they are of elastic nature.

Jelly-like Connective Tissue.

We have now considered connective tissues in which fibres of one or the other kind predominate, and some in which the cells are in preponderance. We come lastly to a form of connective tissue in which the ground substance is in excess of the other histological elements. This is called jelly-like connective tissue. The cells and fibres scattered through it are few and far between. It is found largely in the embryo, notably in the Whartonian jelly, which surrounds and protects the blood-vessels of the umbilical cord. In the adult it is found in the vitreous humour of the eye.

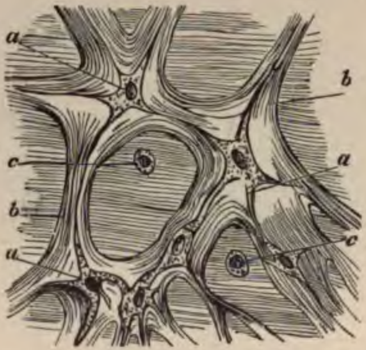


FIG. 73.—Tissue of the jelly of Wharton from umbilical cord. *a*, Connective-tissue corpuscles; *b*, fasciculi of connective-tissue fibres; *c*, spherical cells. (Frey.)

Various points in the structure of the tissue are illustrated in figs. 58 (p. 40) and 73.

The occurrence of large quantities of ground-substance in such tissues has enabled physiologists to examine its chemical nature. Its chief constituents are water, and one or more varieties of mucin, with traces of proteid and mineral salts.

CHAPTER V

THE CONNECTIVE TISSUES (*continued*)

CARTILAGE, BONE, TEETH, BLOOD

Cartilage.

CARTILAGE is popularly termed gristle. It may be divided into two chief kinds: *Hyaline cartilage;* here the matrix or ground substance is clear and free from fibres: *Fibro-cartilage;* here the matrix is pervaded with connective-tissue fibres; when these are of the white variety, the tissue is *white fibro-cartilage;* when they are of the yellow or elastic variety, the tissue is *yellow* or *elastic fibro-cartilage.*

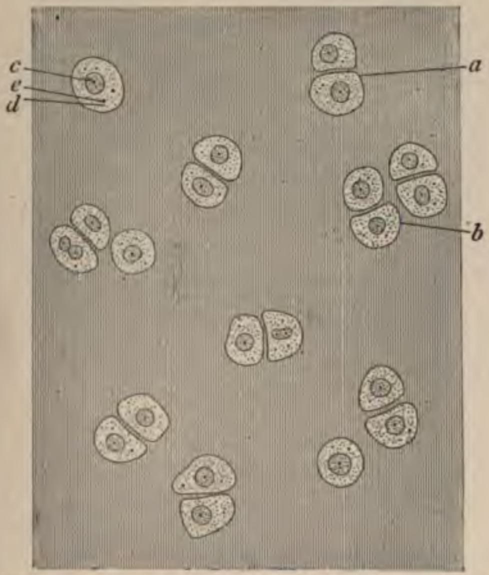


FIG. 74.—Section of articular cartilage. *a*, Group of two cells; *b*, group of four cells; *d*, protoplasm of cell with *e*, fatty granules; *c*, nucleus. (After Schäfer.)

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Hyaline Cartilage is found in the following places:—

1. Covering the articular ends of bones; here it is called *articular cartilage.*

2. Forming the rib-cartilages; here it is called *costal cartilage.*

3. The cartilages of the nose, of the windpipe, of the external auditory meatus, and the greater number of the laryngeal cartilages.

4. *Temporary cartilage:* rods of cartilage which prefigure the majority of the bones in process of development.

Articular cartilage: here the cells are rounded and scattered in groups of two and four through the matrix, which is non-fibrillated (fig. 74), and much firmer than the ground-substance of the connective tissues proper; but it is affected in the same way with silver nitrate.

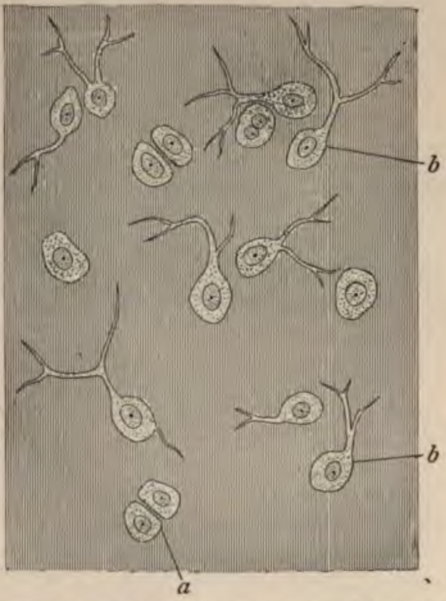

Fig. 75.—Section of transitional cartilage. *a*, Ordinary cartilage cells; *b b*, those with processes. (After Schäfer.)

In the neighbourhood of synovial membranes, the connective-tissue fibres of which extend into the matrix, the cells are branched (*transitional cartilage*), (fig. 75).

The next figure (fig. 76) shows the general arrangement of the cell-groups in a vertical section of articular cartilage. Cartilage is free from blood-vessels, and also from nerves. It is nourished by lymph, but canals connecting the cell-spaces are not evident.

Costal cartilage: here the matrix is not quite so clear, and the cells are larger, more angular, and collected into larger groups than in articular cartilage. Under the *perichondrium*, a fibrous membrane which surrounds the rod of cartilage, the cells are flattened and lie parallel to the surface; in the deeper parts they are irregularly arranged; they frequently contain fat (see fig. 77).

The hyaline cartilages of the nose, larynx, and trachea (fig. 78) resemble costal cartilage.

Hyaline cartilage in many situations (costal, laryngeal, tracheal) shows a tendency to become calcified late in life.

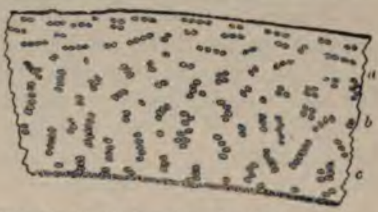

FIG. 76.—Vertical section of articular cartilage; *a*, cell-groups arranged parallel to surface; *b*, cell-groups irregularly arranged; *c*, cell-groups arranged perpendicularly to surface.

On boiling, the ground-substance of cartilage yields a material called *chondrin*. This resembles gelatin very closely, and the differences in its reactions are due to the fact that chondrin is not a chemical individual, but a mixture of gelatin with varying amounts of mucin-like substances.

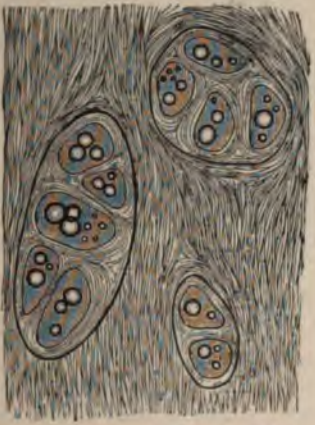

FIG. 77.—Costal cartilage from an adult dog, showing fat-globules in the cartilage-cells. (Cadiat.)

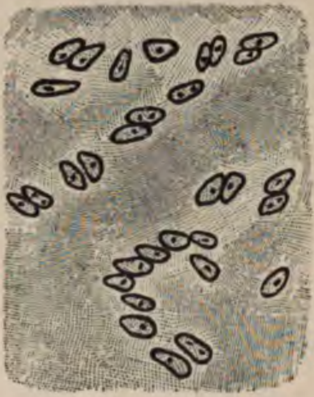

FIG. 78.—Ordinary hyaline cartilage from trachea of a child. The cartilage-cells are enclosed singly or in pairs in a capsule of hyaline substance. × 150 diams. (Klein and Noble Smith.)

White Fibro-Cartilage occurs—

1. As *inter-articular* fibro-cartilage—*e.g.*, the semilunar cartilages of the knee-joint.
2. As *circumferential* or marginal cartilage, as on the edges of the acetabulum and glenoid cavity.
3. As *connecting* cartilage—*e.g.*, the inter-vertebral discs.
4. In the *sheaths of tendons* and sometimes in their substance. In

the latter situation the nodule of fibro-cartilage is called a *sesamoid* fibro-cartilage, of which a specimen may be found in the tendon of the tibialis posticus in the sole of the foot, and usually in the neighbouring tendon of the peroneus longus.

White fibro-cartilage (fig. 79) is composed of cells and a matrix. The latter is permeated by fibres of the white variety.

In this kind of fibro-cartilage it is not unusual to find portions so densely fibrous that no cells can be seen; but in other parts continuous with these, cartilage-cells are freely distributed.

Yellow *or* **Elastic Fibro-Cartilage** is found in the pinna of the external ear, in the epiglottis and cornicula laryngis, and in the Eustachian tube.

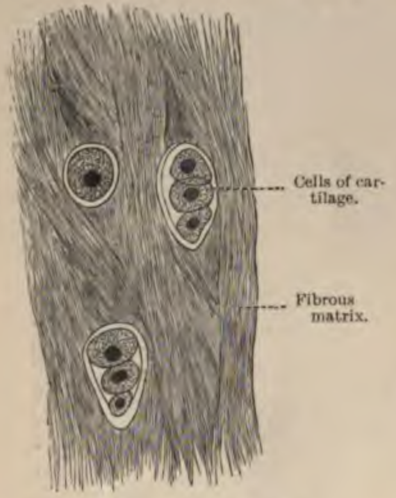

FIG. 79.—White fibro-cartilage. (Cadiat.)

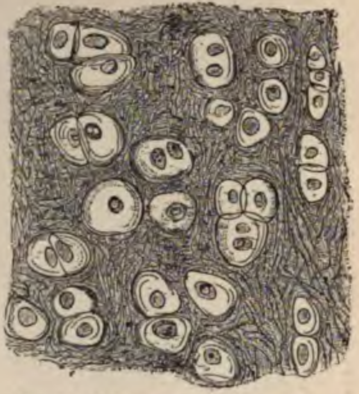

FIG. 80.—Yellow or elastic fibro-cartilage. (Cadiat.)

The cells in this variety of cartilage are rounded or oval, with well-marked nuclei and nucleoli (fig. 80). The matrix in which they are seated is pervaded in all directions by fine elastic fibres, which form an intricate interlacement about the cells: a small and variable quantity of non-fibrillated hyaline intercellular substance is present around the cells.

Development of Cartilage.—Like other connective tissues, cartilage originates from mesoblast; the cells are unbranched, and the disposition of the cells in fully formed cartilage in groups of two, four, etc., is due to the fact that each group has originated from the division of a single cell, first into two, each of these again into two, and so on. This process of cell division is accompanied with the usual karyokinetic changes.

Each cell deposits on its exterior a sheath or capsule; on division each of the daughter-cells deposits a new capsule within this, and the process may be repeated (see fig. 81).

Thus the cells get more and more separated. The fused capsules form a very large part of the matrix, and indications of their previous existence may sometimes be seen in fully formed cartilage by the presence of faint concentric lines around the cells (see fig. 77).

In a variety of cartilage found in the ears of rats and mice called *cellular cartilage*, the cells never multiply to any great extent, and they are only separated by their thickened capsules.

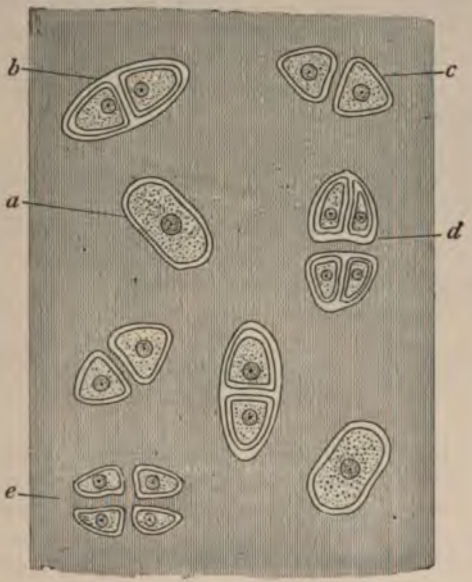

FIG. 81.—Plan of multiplication of cells in cartilage. *a*, Cell in its capsule; *b*, divided into two, each with a capsule; *c*, primary capsule disappeared, secondary capsules coherent with matrix; *d*, tertiary division; *e*, secondary capsules disappeared, tertiary coherent with matrix. (After Sharpey.)

But in most cartilages the cell-capsules will not explain the origin of the whole matrix, but intercellular material accumulates outside the capsules and still further separates the cells.

By certain methods of double staining, this twofold manner of formation may be shown very markedly. We have seen that chondrin obtained by boiling cartilage is really a mixture of two substances; one is a mucinoid material, and comes from the capsules; the other is gelatin, which comes from the rest of the ground-substance which is collagenous. In hyaline cartilage, however, the collagen does not become precipitated to form fibres, but in white fibro-cartilage it does. In yellow fibro-cartilage the matrix is pervaded by a deposit of elastin, which results in the formation of a network of elastic fibres.

Bone.

Bone contains nearly 50 per cent. of water; the solid material is composed of *earthy* and *animal* matter in the proportion of about 67 per cent. of the former to 33 per cent. of the latter. The earthy matter is composed chiefly of *calcium phosphate*, but besides this, there is a small quantity (about 11 of the 67 per cent.) of *calcium carbonate, calcium fluoride*, and *magnesium phosphate.*

The animal matter is chiefly *collagen*, which is converted into *gelatin* by boiling.

The animal and earthy constituents of bone are so intimately blended and incorporated the one with the other that it is only by severe measures, as for instance by a white heat in one case and by the action of concentrated acids in the other, that they can be separated. Their close union too is further shown by the fact that when by acids the earthy matter is dissolved out, or on the other hand when the animal part is burnt out, the shape of the bone is alike preserved.

The proportion between these two constituents of bone varies slightly in different bones in the same individual and in the same bone at different ages.

To the naked eye there appear two kinds of structure in different bones, and in different parts of the same bone, namely, the *dense* or *compact*, and the *spongy* or *cancellous* tissue. Thus, in making a longitudinal section of a long bone, as the humerus or femur, the articular extremities are found capped on their surface by a thin shell of compact bone, while their interior is made up of the spongy or cancellous tissue. The *shaft*, on the other hand, is formed almost entirely of a thick layer of the compact bone, and this surrounds a central canal, the *medullary* cavity—so called from its containing the *medulla* or marrow.

In the flat bones, as the parietal bone or the scapula, the cancellous structure (diploë) lies between two layers of the compact tissue, and in the short and irregular bones, as those of the *carpus* and *tarsus*, the cancellous tissue fills the interior, while a thin shell of compact bone forms the outside.

Marrow.—There are two distinct varieties of marrow—the *red* and *yellow.*

Red marrow is the connective tissue which occupies the spaces in the cancellous tissue; it is highly vascular, and thus maintains the nutrition of the spongy bone, the interstices of which it fills. It contains a few fat-cells and a large number of *marrow-cells.* The marrow-cells are amœboid, and resemble large leucocytes; the granules of some of these cells stain readily with acid and neutral dyes, but a considerable number have coarse granules which stain readily with basic dyes like methylene blue. Among the cells are some nucleated cells of the same tint as coloured blood-corpuscles. These are termed *erythroblasts.* From them the coloured corpuscles of the blood are developed. There are also a few large cells with many nuclei, termed *giant cells* or *myeloplaxes* (fig. 82).

Yellow marrow fills the medullary cavity of long bones, and consists chiefly of fat-cells with numerous blood-vessels; many of its cells also are the colourless marrow-cells first mentioned.

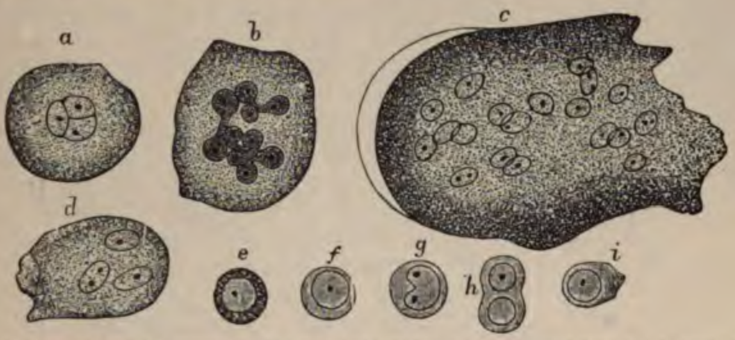

FIG. 82.—Cells of the red marrow of the guinea-pig, highly magnified. *a*, A large cell, the nucleus of which appears to be partly divided into three by constrictions; *b*, a cell, the nucleus of which shows an appearance of being constricted into a number of smaller nuclei; *c*, a so-called giant cell or myeloplaxe, with many nuclei; *d*, a smaller myeloplaxe, with three nuclei; *e*—*i*, proper cells of the marrow. (E. A. Schäfer.)

Periosteum and Nutrient Blood-vessels.—The surfaces of bones, except the part covered with articular cartilage, are clothed by a tough, fibrous membrane, the *periosteum;* and it is from the blood-vessels which are distributed in this membrane, that the bones, especially their more compact tissue, are in great part supplied with nourishment; minute branches from the periosteal vessels enter the little foramina on the surface of the bone, and find their way to the Haversian canals, to be immediately described. The long bones are supplied also by a proper nutrient artery which, entering at some part of the shaft so as to reach the medullary cavity, breaks up into branches for the supply of the marrow, from which again small vessels are distributed to the interior of the bone. Other small blood-vessels pierce the articular extremities for the supply of the cancellous tissue.

Microscopic Structure of Bone.—Notwithstanding the differences of arrangement just mentioned, the structure of all bone is found under the microscope to be essentially the same.

Examined with a rather high power its substance is found to contain a multitude of small irregular spaces, approximately fusiform in shape, called *lacunæ*, with very minute canals or *canaliculi* leading from them, and anastomosing with similar little prolongations from other lacunæ (fig. 83). In very thin layers of bone, no other canals but these may be visible; but on making a transverse section of the compact tissue as of a long bone, *e.g.*, the humerus or ulna, the arrangement shown in fig. 83 can be seen.

The bone seems mapped out into small circular districts, at or about the centre of each of which is a hole, around which is an appearance as of concentric layers; the *lacunæ* and *canaliculi* follow the same concentric plan of distribution around the small hole in the centre, with which indeed they communicate.

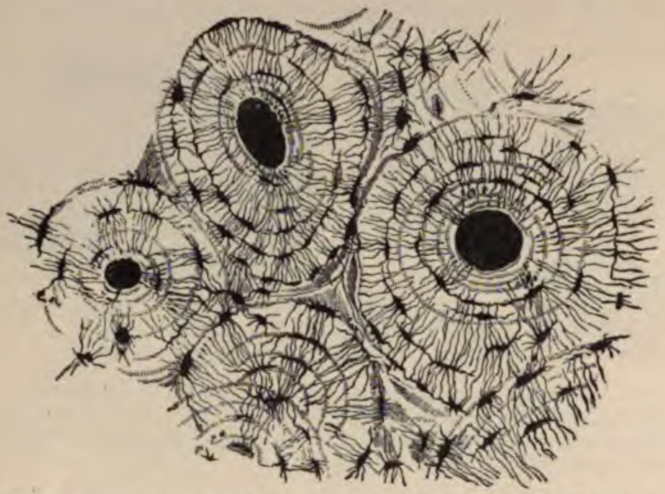

FIG. 83.—Transverse section of compact bony tissue (of humerus). Three of the Haversian canals are seen, with their concentric rings; also the lacunæ, with the canaliculi extending from them across the direction of the lamellæ. The Haversian apertures were filled with air and débris in grinding down the section, and therefore appear black in the figure, which represents the object as viewed with transmitted light. The Haversian systems are so closely packed in this section, that scarcely any *interstitial* lamellæ are visible. × 150. (Sharpey.)

On making a longitudinal section, the central holes are found to be simply the cut extremities of small canals which run lengthwise through the bone, anastomosing with each other by lateral branches (fig. 84); these canals are called *Haversian canals*, after the name of the physician, Clopton Havers, who first accurately described them.

The **Haversian canals**, the average diameter of which is $\frac{1}{500}$ of an inch, contain blood-vessels, and by means of them blood is conveyed to all, even the densest parts of the bone; the minute canaliculi and lacunæ take up the lymph exuded from the Haversian blood-vessels, and convey it to the substance of the bone which they traverse.

The blood-vessels enter the Haversian canals both from without, by traversing the small holes which exist on the surface of all bones beneath the periosteum, and from within by means of small channels which extend from the medullary cavity, or from the cancellous tissue. The arteries and veins usually occupy separate canals, and the veins, which are the larger, often present, at irregular intervals, small pouch-like dilatations. Nerve filaments are also found in the Haversian canals, and a little connective tissue with cleft-like lymph spaces. The larger canals may contain a few marrow cells.

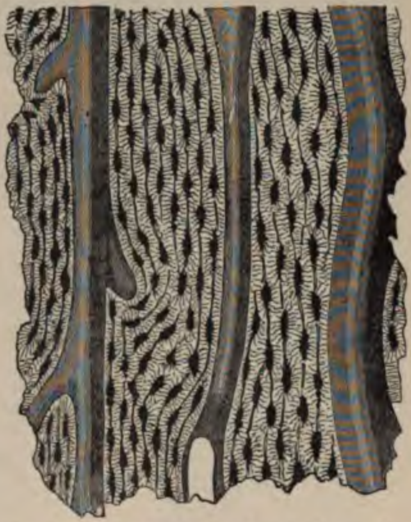
FIG. 84.—Longitudinal section from the human ulna, showing Haversian canals, lacunæ, and canaliculi. (Rollett.)

The **lacunæ** are occupied by branched cells, which are called *bone-cells*, or *bone-corpuscles* (fig. 85); these closely resemble ordinary branched connective-tissue corpuscles. Bone is thus essentially connective tissue, the ground-substance of which is impregnated with lime salts. The bone-corpuscles with their processes, occupying the lacunæ and canaliculi, correspond exactly to the connective-tissue corpuscles lying in branched spaces. The connection of the lacunæ by the canaliculi allows the nutrient lymph to pass from place to place.

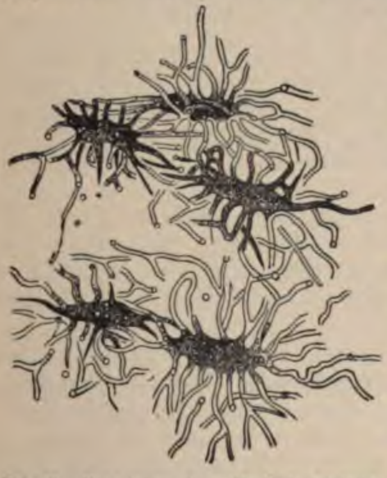
FIG. 85.—Bone-corpuscles with their processes as seen in a thin section of human bone. (Rollett.)

Lamellæ of Compact Bone.—In the shaft of a long bone three distinct sets of lamellæ can be clearly recognised.

1. *Circumferential* lamellæ; these are concentrically arranged just beneath the periosteum, and around the medullary cavity.

2. *Haversian* lamellæ; these

are concentrically arranged around the Haversian canals to the number of six to eighteen around each.

3. *Interstitial* lamellæ; these connect the systems of Haversian lamellæ, filling the spaces between them, and consequently attaining their greatest development where the Haversian systems are few, and *vice versâ*.

The ultimate structure of the lamellæ is fibrous. If a thin film be peeled off the surface of a bone, from which the earthy matter has been removed by acid, and examined with a high power of the microscope, it will be found composed of very slender fibres decussating obliquely, but coalescing at the points of intersection, as if here the fibres were fused rather than woven together (fig. 86). These are called the *intercrossing fibres of Sharpey;* they correspond to the white fibres of connective tissue, and form the source of the gelatin obtained by boiling bone.

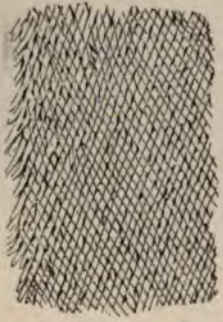

FIG. 86.—Thin layer peeled off from a softened bone. This figure, which is intended to represent the reticular structure of a lamella, gives a better idea of the object when held rather farther off than usual from the eye. × 400. (Sharpey.)

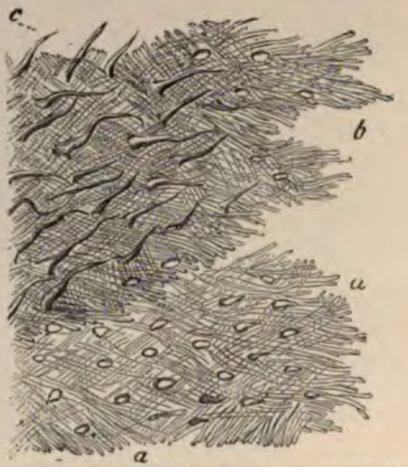

FIG. 87.—Lamellæ torn off from a decalcified human parietal bone at some depth from the surface. *a*, *a*, Lamellæ, showing intercrossing fibres; *b*, darker part, where several lamellæ are superposed; *c*, perforating fibres. Apertures, through which perforating fibres had passed, are seen especially in the lower part, *a*, *a*, of the figure. (Allen Thomson.)

In many cases, as in the parietal bone, the lamellæ are perforated by tapering fibres called the *perforating fibres of Sharpey*, resembling in character the ordinary white or more rarely the elastic fibres, which bolt the neighbouring lamellæ together, and may be drawn out when the latter are torn asunder (fig. 87). These perforating fibres originate from ingrowing processes of the periosteum, and in the adult still retain their connection with it.

Development of Bone.—From the point of view of their development, all bones may be subdivided into two classes:—

(*a.*) Those which are ossified directly or from the first in a fibrous membrane afterwards called the periosteum—*e.g.*, the bones forming the vault of the skull, parietal, frontal, and a certain portion of the occipital bones.

(*b.*) Those whose form, previous to ossification, is laid down in *hyaline cartilage*—*e.g.*, humerus, femur.

The process of development, pure and simple, may be best studied in bones which are not preceded by cartilage; and without a knowledge of this process (ossification in *membrane*), it is impossible to understand the more complex series of changes through which such a structure as the cartilaginous femur of the fœtus passes in its transformation into the bony femur of the adult (ossification in *cartilage*).

Ossification in Membrane.—The membrane, afterwards forming the periosteum, from which such a bone as the parietal is developed, consists of two layers—an external *fibrous*, and an internal *cellular* or *osteo-genetic*.

The external layer is made up of ordinary fibrous tissue. The internal layer consists of a network of fine fibrils with a large number of nucleated cells (*osteoblasts*), some of which are oval, others drawn out into long branched processes: it is more richly supplied with capillaries than the outer layer. It is this portion of the periosteum which is immediately concerned in the formation of bone.

In such a bone as the parietal, ossification is preceded by an increase in the vascularity of this membrane, and then spicules, starting from a *centre of ossification* near the centre of the future bone, shoot out in all directions towards the periphery. These primary bone spicules consist of fibres which are termed *osteo-genetic fibres;* they are composed of a soft, transparent substance called *osteogen*, around and between which calcareous granules are deposited. The fibres in their precalcified state are likened to bundles of white fibrous tissue, to which they are similar in chemical composition, but from which they differ in being stiffer and less wavy. The deposited granules after a time become so numerous as to imprison the fibres, and bony spiculæ result. By the junction of the osteo-genetic fibres and their resulting bony spicules a meshwork of bone is formed. The osteogenetic fibres, which become indistinct as calcification proceeds, persist in the lamellæ of adult bone as the intercrossing fibres of Sharpey. The osteoblasts, being in part retained within the bony layers thus produced, form bone corpuscles. On the bony trabeculæ first formed, layers of osteoblastic cells from the osteo-genetic layer of the periosteum repeat the process just described; and as this occurs in several thicknesses, and also at the edges of the spicules previously formed, the bone increases, both in thickness, length and breadth. The process is not completed by the time the child is born; hence the fontanelles or still soft places on the heads of infants. Fig. 88 represents a small piece of the growing edge of a parietal bone.

The bulk of the primitive spongy bone is in time converted into compact bony tissue, with Haversian systems. Those portions in the interior not converted into bone become filled with the red marrow of the cancellous tissue.

Ossification in Cartilage.—Under this heading, taking the femur or any other long bone as an example, we have to consider the process by which the solid cartilaginous rod which represents the bone in the fœtus is converted into the hollow cylinder of compact bone with expanded ends formed of cancellous tissue of which the adult bone is made up. We must bear in mind the fact that this fœtal cartilaginous femur is many times smaller than even the medullary cavity of the shaft of the mature bone, and, therefore, that not a trace of the original cartilage can be present in the femur of the adult. Its purpose is indeed purely temporary; and, after its calcification, it is gradually and entirely absorbed.

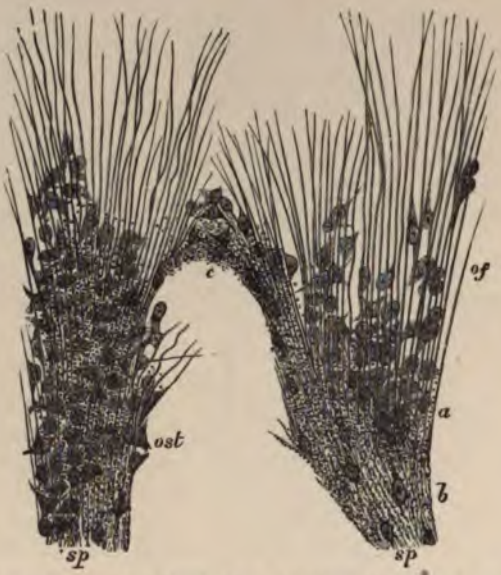

FIG. 88.—Part of the growing edge of the developing parietal bone of a fœtal cat. *sp*, Bony spicules with some of the osteoblasts imbedded in them, producing the lacunæ; *of*, osteogenic fibres prolonging the spicules with osteoblasts (*ost*) between them and applied to them. (Schäfer.)

The cartilaginous rod which forms the precursor of a fœtal long bone is sheathed in a membrane termed the *perichondrium*, which exactly resembles the periosteum described above; it consists of two layers, in the deeper one of which spheroidal and branched cells predominate and blood-vessels abound, while the outer layer consists mainly of fibres.

Between the cartilaginous prefigurement of which the fœtal long bone consists and the adult bone there are several intermediate stages.

The process may, however, be most conveniently described as occurring in three principal stages.

The first stage consists of two sets of changes, one in the cartilage, the other under the perichondrium. These take place side by side. In the cartilage the cells in the middle * become enlarged and separated from one another. The cartilage-cells on each side get arranged in rows in the direction of the extremities of the cartilaginous rod. If at this stage one cuts the little embryonic bone with a knife, the knife encounters resistance, and there is a sensation of grittiness. This is due to the fact that calcareous particles are deposited in the matrix; and in consequence of this the matrix stains differently with histological reagents from the unaltered matrix. Simultaneously with this, the periosteal tissue is forming layer after layer of true bone; this is formed exactly in the same way

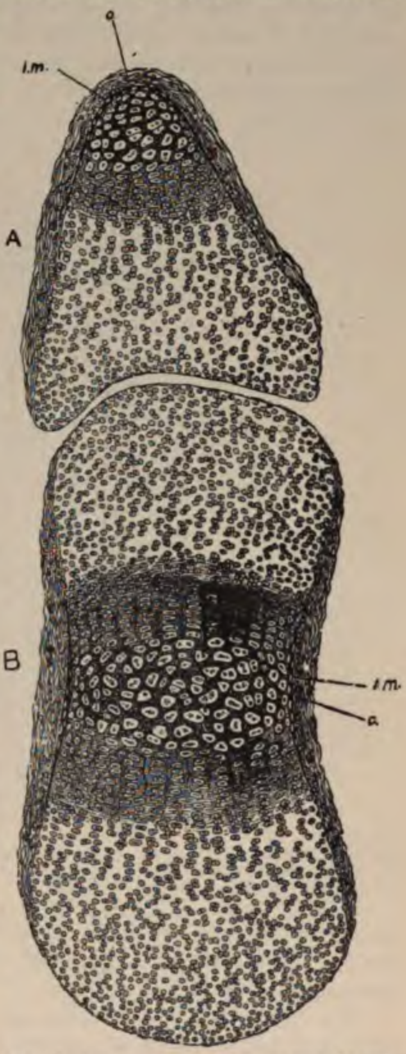

FIG. 89.—Section of two fœtal phalanges; the cartilage-cells in the centre of B are enlarged and separated from one another by calcified matrix. *im*, Layer of bone deposited under the periosteum; *o*, layer of osteoblasts by which this layer was formed. The rows of cartilage-cells are seen on each side of the centre of calcification. In A, the terminal phalanx, the changes begin at the tip. (After Dixey.)

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* This is the case in nearly all the long bones, but in the terminal phalanges the change occurs first, not in the middle but at their distal extremities.

as in such a bone as the parietal; by the agency of the osteoblasts, osteogenetic fibres, and] then spicules of bone, are formed by deposit of calcareous matter. As the layers are formed, some of the osteoblasts get walled in between the layers, and become bone cells.

In the later part of this stage the calcareous deposit between the cartilage-cells cuts them off from nutrition, and they in consequence waste, leaving spaces that are called the *primary areolæ.* The calcareous deposit creeps up between the rows of cartilage-cells, enclosing them in calcified boxes containing one, two, or more cells each. The wasting of the cells leads here also to the formation of primary areolæ.

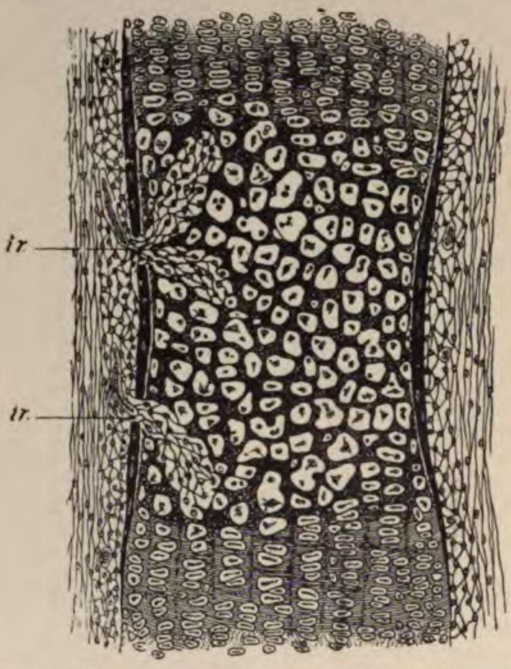

FIG. 90.—Ossification in cartilage showing stage of irruption. The shrunken cartilage-cells are seen in the primary areolæ. At *ir* an irruption of the subperiosteal tissue has penetrated the subperiosteal bony crust. (After Lawrence.)

We may roughly compare the two sets of cells engaged in the process to two races of settlers in a new country. The cartilage-cells constitute one race, and so successfully build for themselves calcareous homes as to be completely boxed up; so they waste and disappear, leaving only the walls of their homes enclosing the spaces called primary areolæ. The osteoblasts, the other race of cells under the perichondrium, are forming layers of true bone in that situation.

Some, it is true, get walled in in the process, and become bone-corpuscles, but the system of intercommunicating lacunæ and canaliculi maintains their nutrition.

These two races are working side by side, and at first do not interfere with each other. But soon comes a declaration of war, and we enter upon the *second stage* of ossification, which is very appropriately called the *stage of irruption* (fig. 90). Breaches occur in the bony wall which the osteoblasts have built like a girdle round the calcifying cartilage, and through these the perichondrial tissue pours an invading army into the calcified cartilage. This consists of *osteoblasts*, the bone formers; *osteoclasts*, or the bone destroyers; the latter are large cells, similar to the myeloplaxes found in marrow (fig. 82). There are also a few fibres, and a store of nutrient supply in the shape of blood-vessels.

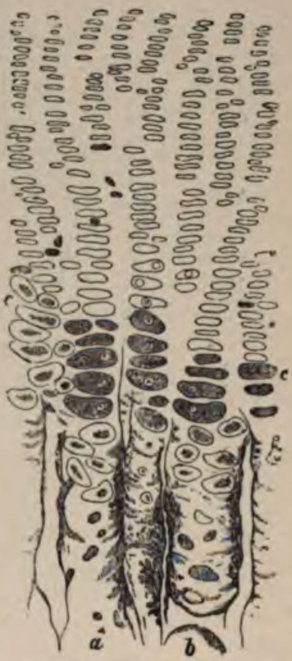

FIG. 91.—Longitudinal section of ossifying cartilage. Calcified trabeculæ are seen extending between the columns of cartilage-cells. *c*, Cartilage-cells; *a*, *b*, secondary areolæ. × 140. (Sharpey.)

Having got inside, the osteoclasts set to work to demolish the homes of the cartilage-cells, the walls of the primary areolæ, and thus large spaces are formed, which are called the *secondary areolæ*, or the *medullary spaces*. On the ruins of the calcified cartilage, the osteoblasts proceed to deposit true bone in layers, just as they were wont to do in their own country, under the periosteum.

The third stage of ossification is a repetition of these two stages towards the extremities of the cartilage. The cartilage-cells get flattened and arranged in rows; calcareous deposit occurs around these, and primary areolæ result; then follows the advance of the subperiosteal tissue, the demolition of the primary areolæ, the formation of secondary areolæ, and the deposit of true bone. At the same time, layer upon layer is still being deposited beneath the periosteum, and these, from being at first a mere girdle round the waist of the bone, now extend towards its extremities.

The next figure (fig. 91) is a magnified view of the line of advance.

The bone which is first formed is less regularly lamellar than that of the adult. The lamellæ are not deposited till after birth, and their formation is preceded by a considerable amount of absorption.

To carry our simile further, the osteoblasts are not satisfied with the rough constructions that they were first able to make, but having exterminated the cartilage, they destroy (again through the agency of the regiment of giant osteoclasts) their first work, and build regular lamellæ, leaving lacunæ for the accommodation of those who desire to retire from active warfare.

About this time, too, the marrow cavity is formed by the absorption of the bony tissue that originally occupied the centre of the shaft. Here the osteoclasts have again to do the work, and, with this final act of destruction, all remains of any calcified cartilage of the fœtal bone entirely disappear.

The formation of a so-called cartilage bone is thus, after all, a formation of bone by subperiosteal tissue, just as it is in the so-called membrane bone.

After a time the cartilage at the ends of the shaft begins to ossify independently, and the epiphyses are formed. They are not joined on to the shaft till late in life, so that growth of the bone in length can continue till union takes place.

Bone grows in width by the deposition of layers under the periosteum, like successive rings formed under the bark of a growing tree. This was shown long before the histological details which we have described were made out by Sharpey. Silver rings were placed by Duhamel around the bones of young pigeons. When killed later, the rings were completely covered in by bone; and in the animals killed last, were even found in the central cavity. Another series of experiments with pigs was made by the celebrated John Hunter. The young animals were fed alternately on ordinary food and food dyed by the red pigment madder. The new bony tissue acts like what dyers called a "mordant": it fixes the dye, and the rings of bone deposited during the madder periods were distinctly red in colour.

The importance of the periosteum in bone formation is now recognised by surgeons. When removing a piece of bone they are careful, if possible, to leave the periosteum behind: this leads to regeneration of the lost bone. If it is absolutely necessary to remove the periosteum, successful cases have occurred in which the living periosteum from an animal has effectively been transplanted.

The Teeth.

During the course of his life, man, in common with most other mammals, is provided with two sets of teeth; the first set, called the *temporary* or *milk-teeth*, makes its appearance in infancy, and is in the course of a few years shed and replaced by the second or *permanent* set.

The **temporary** or **milk-teeth** have only a very limited term of existence.

They are ten in number in each jaw, namely, on either side from the middle line two *incisors*, one *canine*, and two deciduous *molars*, and are replaced by ten permanent teeth. The number of permanent teeth in each jaw is, however, increased to sixteen by the development of three molars on each side of the jaw, which are called the permanent or true molars.

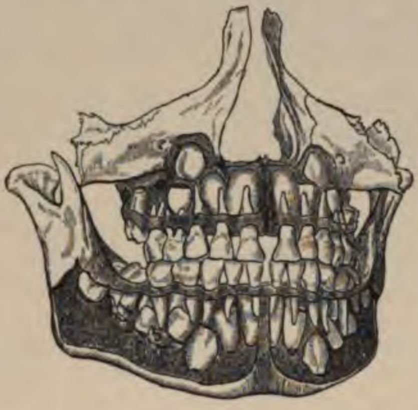

FIG. 92.—Normal well-formed jaws, from which the alveolar plate has been in great part removed, so as to expose the developing permanent teeth in their crypts in the jaws. (Tomes.)

The following formula shows, at a glance, the comparative arrangement and number of the temporary and permanent teeth:—

Temporary Teeth.

MIDDLE LINE OF JAW.

MOLARS.	CANINE.	INCISORS.	INCISORS.	CANINE.	MOLARS.	
2	1	2	2	1	2=10	=20
2	1	2	2	1	2=10	

Permanent Teeth.

MIDDLE LINE OF JAW.

TRUE MOLARS.	BICUSPIDS OR PRE-MOLARS.	CANINE.	INCISORS.	INCISORS.	CANINE.	BICUSPIDS OR PRE-MOLARS.	TRUE MOLARS.
3	2	1	2	2	1	2	3
3	2	1	2	2	1	2	3

From this formula it will be seen that the two bicuspid or premolar teeth in the adult are the successors of the two deciduous molars in the child. They differ from them, however, in some respects, the *temporary* molars having a stronger likeness to the *permanent* than to their immediate descendants the so-called bicuspids, besides occupying more space in the jaws.

The temporary incisors and canines differ from their successors but little except in their smaller size and the abrupt manner in which their enamel terminates at the necks of the teeth, forming a ridge or thick edge. Their colour is more of a bluish-white than of a yellowish shade.

The following tables show the average times of eruption of the Temporary and Permanent teeth. In both cases the eruption of any given tooth of the lower precedes, as a rule, that of the corresponding tooth of the upper jaw.

Temporary or Milk Teeth.

The figures indicate in months the age at which each tooth appears.

INCISORS.	DECIDUOUS FIRST MOLARS.	CANINES.	DECIDUOUS SECOND MOLARS.
6	12	18	24

Permanent Teeth.

The age at which each tooth is cut is indicated in this table in years.

FIRST MOLARS.	INCISORS.		BICUSPIDS OR PRE-MOLARS.		CANINES.	SECOND MOLARS.	THIRD MOLARS OR WISDOMS.
	CENTRALS.	LATERALS.	FIRST.	SECOND.			
6	7	8	9	10	11	12	17 to 25

The times of eruption given in the above tables are only approximate: the limits of normal variation are tolerably wide. Certain diseases affecting the bony skeleton, *e.g.* Rickets, retard the eruptive period considerably.

It is important to notice that it is a molar which is the first tooth to be cut in the permanent dentition, not an incisor as in the case of the temporary set, and also that it appears *behind* the last deciduous molar on each side.

The third molars, often called *Wisdoms*, are sometimes unerupted through life from want of sufficient jaw space and the presence of the other teeth; cases of whole families in which their absence is a characteristic feature are occasionally met with.

When the teeth are fully erupted it will be observed that the upper incisors and canines project obliquely over the lower front teeth, and the external cusps of the upper bicuspids and molars lie outside those of the corresponding teeth in the lower jaw. This arrangement allows to some extent of a scissor-like action in dividing and biting food in the case of incisors; and a grinding motion in that of the bicuspids and molars when the side to side movements of the lower jaw bring the external cusps of the lower teeth into direct articulation with those of the upper, and then cause them to glide down the inclined surfaces of the external and up the internal cusps of these same upper teeth during the act of mastication.

The work of the canine teeth in man is similar to that of his incisors. Besides being a firmly implanted tooth and one of stronger substance than the others, the canine tooth is important in preserving the shape of the angle of the mouth, and by its shape, whether pointed or blunt, long or short, it becomes a character tooth of the dentition as a whole in both males and females.

Another feature in the fully developed and properly articulated set of teeth is that no two teeth oppose each other only, but each tooth is in opposition with two, except the upper Wisdom, usually a small tooth. This is the result of the greater width of the upper incisors, which so arranges the "bite" of the other teeth that the lower canine closes in front of the upper one.

Should a tooth be lost, therefore, it does not follow that its former opponent remaining in the mouth is rendered useless and thereby liable to be removed from the jaw by a gradual process of extrusion commonly seen in teeth that have no work to perform by reason of absence of antagonists.

Structure of a Tooth.

A tooth is generally described as possessing a *crown*, *neck*, and *root*.

The *crown* is the portion which projects beyond the level of the gum. The *neck* is that constricted portion just below the crown which is embraced by the free edges of the gum; and the *root* includes all below this.

On making longitudinal and transverse sections through its centre (figs. 93, 94), a tooth is found to be composed of a hard material, *dentine* or ivory, which is moulded around a central cavity which resembles in general shape the outline of the tooth; the cavity is called the *pulp* cavity from its containing the very vascular and sensitive pulp.

The *tooth-pulp* is composed of loose connective tissue, blood-vessels, nerves, and large numbers of cells of varying shapes; on the surface in close connection with the dentine is a specialised layer of cells called *odontoblasts,* which are elongated columnar cells with a large nucleus at the tapering ends farthest from the *dentine.*

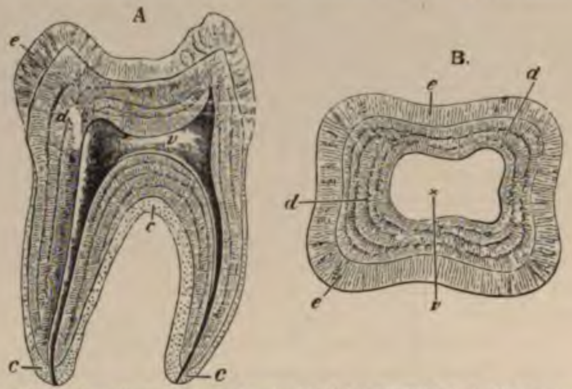

FIG. 93.—A, Longitudinal section of a human molar tooth; *c*, cement; *d*, dentine; *e*, enamel; *v*, pulp-cavity. (Owen.)
B, Transverse section. The letters indicate the same as in A.

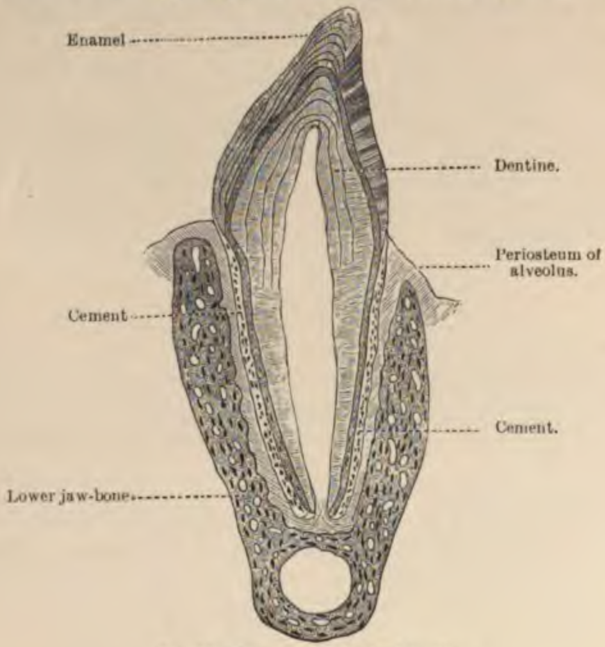

FIG. 94.—Premolar tooth of cat *in situ.*

The blood-vessels and nerves enter the pulp through a small opening at the apical extremity of each root. The exact terminations of the nerves are not definitely known. They have never been observed to enter the dentinal tubes. No lymphatics have been seen in the pulp.

A layer of very hard calcareous matter, the *enamel*, caps that part of the dentine which projects beyond the level of the gum; while sheathing the portion of dentine which is beneath the level of the gum, is a layer of true bone, called the *cement* or *crusta petrosa*.

At the neck of the tooth, where the enamel and cement come into contact, each is reduced to an exceedingly thin layer; here the cement overlaps the enamel, and is prolonged over it. On the surface of the crown of the tooth, when it first comes through the jaw, is a thin membrane called *Nasmyth's membrane*, or the *cuticle* of the tooth. The covering of enamel becomes thicker towards the crown, and the cement towards the lower end or apex of the root.

Dentine or *Ivory*.

Dentine closely resembles bone in chemical composition. It contains, however, only 10 per cent. of water. The proportion in a hundred parts of the solids is about twenty-eight *animal* to seventy-two of *earthy* matter. The former, like the animal matter of bone, may be converted into *gelatin* by boiling. It also contains a trace of fat. The earthy matter is made up chiefly of *calcium phosphate*, with a small portion of the *carbonate*, and traces of *calcium fluoride* and *magnesium phosphate*.

Under the microscope dentine is seen to be finely channelled by a multitude of delicate tubes, which by their inner ends communicate with the pulp-cavity, and by their outer extremities come into contact with the under part of the enamel and cement, and sometimes even penetrate them for a greater or less distance (figs. 95, 97). The matrix in which these tubes lie is composed of "a reticulum of fine fibres of connective tissue modified by calcification, and where that process is complete, entirely hidden by the densely deposited lime salts" (Mummery).

In their course from the pulp-cavity to the surface, the minute tubes form gentle and nearly parallel curves, and divide and subdivide dichotomously, but without much lessening of their calibre until they approach their peripheral termination.

From their sides proceed other exceedingly minute secondary canals, which extend into the dentine between the tubules and anastomose with each other. The tubules of the dentine, the average diameter of which at their inner and larger extremity is $\frac{1}{4500}$ of an inch, contain fine prolongations from the tooth-pulp, which give the dentine a certain faint sensitiveness under ordinary circumstances, and, without doubt, have to do also with its nutrition. These prolongations from the tooth-pulp are processes of the dentine-cells or *odontoblasts,* the columnar cells lining the pulp-cavity; the relation of these processes to the tubules in which they lie is precisely similar to that of the processes of the bone-corpuscles to the canaliculi of bone. The outer portion of the dentine, underlying the cement, and the enamel to a much lesser degree, forms a more or less distinct layer termed the *granular* or *interglobular* layer (fig. 95). It is characterised by the presence of a number of irregular minute cavities. The explanation of these will be seen when we study the development of a tooth.

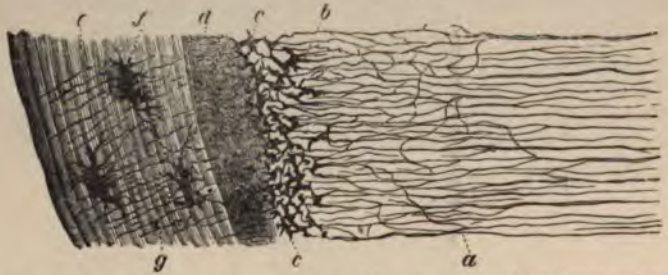

FIG. 95.—Section of a portion of the dentine and cement from the middle of the root of an incisor tooth. *a*, Dentinal tubules ramifying and terminating, some of them in the interglobular spaces *b* and *c*; *d*, inner layer of the cement with numerous closely set canaliculi; *e*, outer layer of cement; *f*, lacunæ; *g*, canaliculi. × 350. (Kölliker.)

Enamel.

Enamel is by far the hardest tissue in the body; it is composed of the same inorganic compounds that enter into the composition of

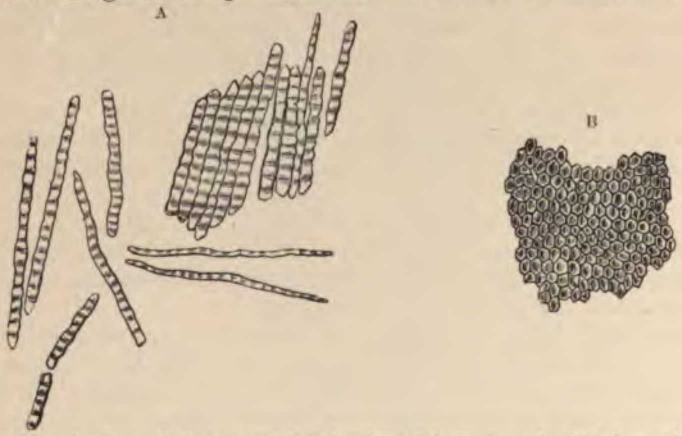

FIG. 96.—Enamel prisms. A, fragments and single prisms of the transversely-striated enamel, isolated by the action of hydrochloric acid. B, surface of a small fragment of enamel, showing the hexagonal ends of the fibres with darker centres. × 350. (Kölliker.)

dentine and bone. According to Tomes, it contains no animal matter at all and only 2 or 3 per cent. of water. Gelatin is a characteristic product of connective tissue, and enamel is not a connective tissue, but is epithelial in origin.

Examined under the microscope, enamel is found composed of six-sided prisms (figs. 96, 97) $\frac{1}{5000}$ of an inch in diameter, which are set on end on the surface of the dentine, and fit into corresponding depressions in the same.

They radiate in such a manner from the dentine that at the top of the tooth they are more or less vertical, while towards the sides they tend to the horizontal direction. Like the dentine tubules, they are not straight, but disposed in wavy and parallel curves. The prisms are marked by transverse lines and are solid.

The enamel prisms are connected together by a very minute quantity of hyaline cement substance. In the deeper part of the enamel, between the prisms, are often small *lacunæ*, which have the processes or fibrils lying in the dentinal tubes in connection with them (fig. 97, *c*).

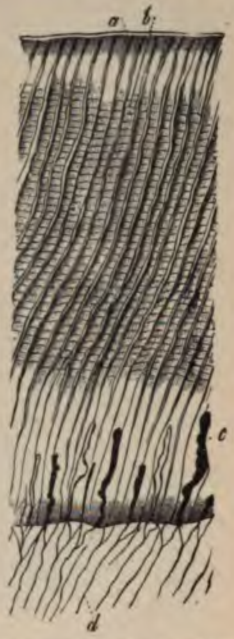

FIG. 97.—Thin section of the enamel, and a part of the dentine. *a*, Cuticular pellicle of the enamel (Nasmyth's membrane); *b*, enamel columns with fissures between them and cross striæ; *c*, larger cavities in the enamel, communicating with the extremities of some of the dentinal tubules (*d*). × 350. (Kölliker.)

Crusta Petrosa.

The *crusta petrosa* or *cement* (fig. 95, *e*, *d*) is composed of true bone, and in it are lacunæ (*f*) and canaliculi (*g*), which sometimes communicate with the outer finely branched ends of the dentinal tubules, and generally with the interglobular spaces. Its laminæ are bolted together by perforating fibres like those of ordinary bone (Sharpey's fibres). Cement differs from ordinary bone in possessing no Haversian canals, or, if at all, only in the thickest part. Such canals are more often met with in teeth with the cement hypertrophied than in the normal tooth.

Development of the Teeth.

The first step in the development of the teeth consists in a downward growth (fig. 98, A, 1) from the deeper layer of stratified epithelium of the mucous membrane of the mouth, which first becomes thickened in the neighbourhood of the maxillæ or jaws now in the course of formation. This process passes downward into a recess of the imperfectly developed tissue of the embryonic jaw. The downward epithelial growth forms the *common enamel* or *dental germ*, and its position is indicated by a slight groove in the mucous membrane of the jaw. After this there is an increased development at certain points corresponding to the situations of the future milk-teeth. The common enamel germ thus becomes extended by further growth into a number of *special enamel germs* (fig. 98, B,) corresponding to each of the milk-teeth, and connected to the common germ by a narrow neck (*f*). Each tooth is thus placed in its own special recess in the embryonic jaw.

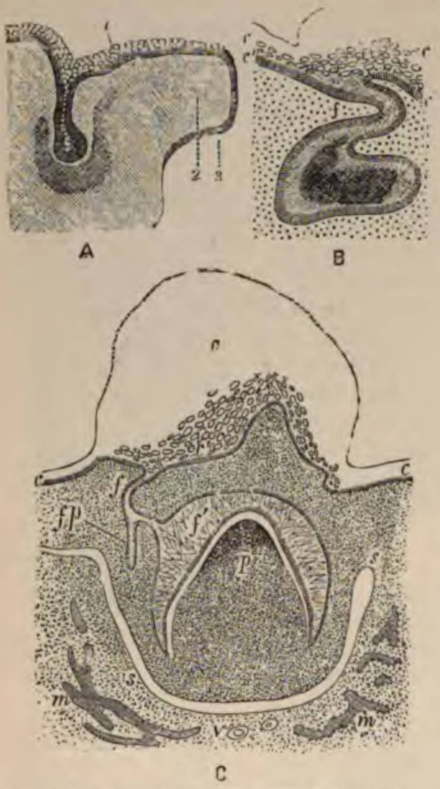

FIG. 98.—Section of the upper jaw of a fœtal sheep. A.—1, common enamel germ dipping down into the mucous membrane; 2, palatine process of jaw; 3, Rete Malpighi. B.—Section similar to A, but passing through one of the special enamel germs here becoming flask-shaped; *c*, *c′*, epithelium of mouth; *f*, neck; *f′*, body of special enamel germ. C.—A later stage; *c*, outline of epithelium of gum; *f*, neck of enamel germ; *f′*, enamel organ; *p*, papilla; *s*, dental sac forming; *f p*, the enamel germ of permanent tooth; *m*, bone of jaw; *v*, vessels cut across. (Waldeyer and Kölliker.)

As these changes proceed, there grows up from the underlying connective tissue into each enamel germ (fig. 98, C, *p*), a distinct vascular papilla (*dental papilla*), and upon it the enamel germ becomes moulded, and presents the appearance of a cap of two layers of epithelium separated by an interval (fig. 98, C, *f*). Whilst part of the subepithelial tissue is elevated to form the dental papilla, the part which bounds the embryonic teeth forms the dental sac (fig. 98, C, *s*); and the rudiment of the jaw sends up processes forming partitions between the teeth. In this way small chambers are produced in which the dental sacs are contained, and thus the sockets of the teeth are formed. The papilla is composed of nucleated cells arranged in a mesh-work of connective tissue, the outer or peripheral part being covered with a layer of columnar nucleated cells called *odontoblasts*.

These cells either by secretion, or as some think by direct transformation of the outer part of each, form a layer of dentinal matrix on the apex of the papilla, or if the tooth has more than one cusp, then at the apex of each cusp. This layer is first uncalcified (*odontogen*), but globules of calcareous matter soon appear in it. These, becoming more numerous, blend into the first cap of dentine. In the meanwhile the odontoblasts have formed a second layer of odontogen within this (fig. 99), and this in turn becomes calcified; thus layer after layer is formed, each extending laterally further than its predecessor; the layers blend except in some places; here portions of odontogen remain, which in a tooth macerated for histological purposes get destroyed, and appear as the *interglobular spaces* (fig. 95), so called because bounded by the deposit of calcareous salts, which occurs, as we have already seen, in the form of globules.

As the odontoblasts retire towards the centre, depositing layer after layer of dentine, they leave behind them long filaments of their protoplasm around which the calcareous deposit is moulded; thus the dentinal tubules occupied by the processes of the odontoblasts are formed.

The other cells of the dental papilla form the cells of the pulp.

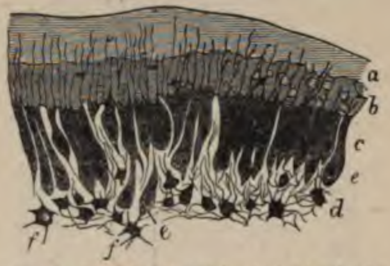

Fig. 99.—Part of section of developing tooth of a young rat, showing the mode of deposition of the dentine. Highly magnified. *a*, Outer layer of fully formed dentine; *b*, uncalcified matrix with one or two nodules of calcareous matter near the calcified parts; *c*, odontoblasts sending processes into the dentine; *d*, pulp; *e*, fusiform or wedge-shape cells found between odontoblasts; *f*, stellate cells of pulp in fibrous connective tissue. The section is stained with carmine, which colours the uncalcified matrix but not the calcified part. (E. A. Schäfer.)

Formation of the enamel.—The portion of the enamel or dental germ that covers the dental papilla is at this stage called the *enamel organ*. This consists of four parts (see figs. 100 and 101).

1. A layer of columnar epithelium cells in contact with the dentine. These are called the *enamel cells*, or *adamantoblasts*.
2. Two or three layers of smaller polyhedral nucleated cells, *the stratum intermedium* of Hannover.
3. A matrix of non-vascular jelly-like tissue containing stellate cells.
4. An outer membrane of several layers of flattened epithelium cells.

The first three layers on an enlarged scale are seen in fig. 101.

The enamel prisms are formed by the agency of the ends of the adamantoblasts which abut on the dental papilla. Each forms a fine deposit of globules staining with osmic acid and resembling keratin in its resistance to mineral acid. At one time it was believed that each adamantoblast was itself calcified and converted into an enamel prism, but this view has been disproved by recent research. The layer of keratin-like material is outside the bodies of the cells, although a process of each adamantoblast extends into it as a tapering fibre (process of Tomes), and it is usually produced simultaneously with the first layer of uncalcified dentine; when it undergoes calcification, the first layer of enamel is complete. The adamantoblasts then repeat the process, first causing a deposition of keratin-like material, and this in turn is calcified, and so on. During the formation of layer after layer of enamel, the adamantoblasts retire. By the time the enamel is approaching completion the other layers of the enamel organ have almost disappeared, and they entirely disappear when the tooth emerges through the gum. But for some little time there is a somewhat more persistent membrane covering the crown; this is Nasmyth's membrane, or the *enamel cuticle;* this is the last formed keratinous layer of enamel which has remained uncalcified.

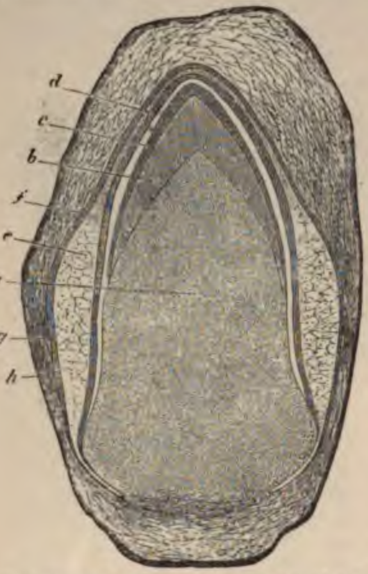

FIG. 100.—Vertical transverse section of the dental sac, pulp, etc., of a kitten. *a*, Dental papilla or pulp; *b*, the cap of dentine formed upon the summit; *c*, its covering of enamel; *d*, inner layer of epithelium of the enamel organ; *e*, gelatinous tissue; *f*, outer epithelial layer of the enamel organ; *g*, inner layer, and *h*, outer layer of dental sac. × 14. (Thiersch.)

As with the dentine, the formation of enamel appears first on the apex of each cusp.

The *cement* or *crusta petrosa* is formed from the internal tissue of the tooth sac, the structure and function of which are identical with those of the osteogenetic layer of the periosteum; or, in other words, ossification in membrane occurs in it.

The outer layer or portion of the membrane of the tooth sac forms the *dental periosteum.*

This periosteum, when the tooth is fully formed, is not only a means of attachment of the tooth to its socket, but also in conjunction with the *pulp* a source of nourishment to it. Additional laminæ of cement are added to the root from time to time during the life of the tooth (as is especially well seen in the abnormal condition called an *exostosis*), by the process of ossification taking place in the periosteum. On the other hand, absorption of the root (such as occurs when the milk-teeth are shed) is due to the action of the osteoclasts of the same membrane.

In this manner the first set of teeth, or the milk-teeth, are formed; and each tooth, as it grows, presses at length on the wall of the sac enclosing it, and, causing its absorption, is *cut*, to use a familiar phrase.

The *temporary* or *milk-teeth* are later replaced by the growth of the permanent teeth, which push their way up from beneath them.

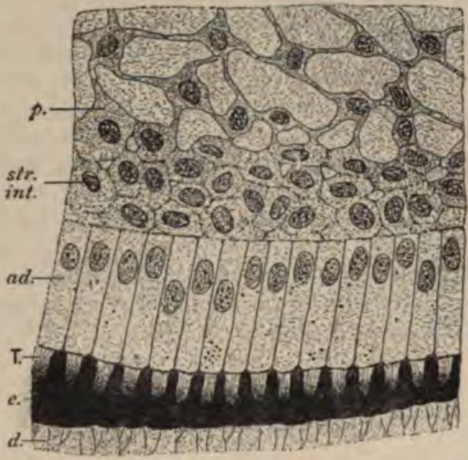

FIG. 101.—Highly magnified view of a piece of the enamel organ in a kitten's canine. *d*, Superficial layer of dentine. *e*, Newly formed enamel stained black by osmic acid. T, Tomes' processes from the adamantoblasts, *ad.*; *str. int.*, stratum intermedium of the enamel organ. *p*, Branched cells of the enamel pulp. (After Röse.)

Each temporary tooth is replaced by a tooth of the permanent set which is developed from a small sac which was originally an offshoot from the sac of the temporary tooth which precedes it, and called the *cavity of reserve* (fig. 98, C, *fp*). Thus the temporary incisors and canines are succeeded by the corresponding permanent ones, the temporary first molar by the first bicuspid; the temporary second molar develops two offshoots, one for the second bicuspid, the other for the permanent first molar. The permanent second molar is budded off from the first permanent molar, and the wisdom from the permanent second molar.

The development of the temporary teeth commences about the sixth week of intra-uterine life, after the laying down of the bony structure of the jaws. Their permanent successors begin to form about the sixteenth week of intra-uterine life. The second permanent molars originate about the third month after birth, and the wisdom teeth about the third year.

The Blood.

A full consideration of the blood will come later, when we know more about the chemical aspects of physiology, but it will be impossible to discuss all the other phenomena we shall have to study in the meanwhile without some elementary knowledge of the principal properties of this fluid. For that reason, and also to complete our list of the connective tissues, we may here rapidly and briefly enumerate its principal characters.

The blood is a fluid which holds in suspension large numbers of solid particles which are called the *corpuscles*. The fluid itself is called the *plasma* or *liquor sanguinis*. It is a richly albuminous fluid; and one of the proteids in it is called *fibrinogen*.

After blood is shed it rapidly becomes viscous, and then sets into a jelly. The jelly contracts and squeezes out of the clot a straw-coloured fluid called *serum*, in which the shrunken clot then floats.

The formation of threads of a solid proteid called *fibrin* from the soluble proteid we have called *fibrinogen* is the essential act of coagulation; this, with the corpuscles it entangles, is called the *clot*. Serum is plasma *minus* fibrin. The following scheme shows the relationships of the constituents of the blood at a glance:—

$$\text{Blood}\begin{cases}\text{Plasma} & \begin{cases}\text{Serum}\\ \text{Fibrin}\end{cases}\\ \text{Corpuscles} & \end{cases}\Big\}\ \text{Clot.}$$

The corpuscles are of two chief kinds, the red and the white. The white corpuscles are typical animal cells, and we have already made their acquaintance when speaking about amœboid movements.

The red corpuscles are much more numerous than the white, averaging in man 5,000,000 per cubic millimetre, or 400 to 500 red to each white corpuscle. It is these red corpuscles that give the red colour to the blood. They vary in size and structure in different groups of the vertebrates. In mammals they are biconcave (except in the camel tribe, where they are biconvex) non-nucleated discs, in man $\frac{1}{3200}$ inch in diameter; during fœtal life nucleated red corpuscles are, however, found. In birds, reptiles, amphibians and fishes they are biconvex oval discs with a nucleus: they are largest in the amphibia. The most important and abundant of the constituents of the red corpuscles is the pigment which is called *hæmoglobin*. This is a proteid-like substance, but is remarkable as it contains a small amount of iron (about 0·4 per cent.).

The blood during life is in constant movement. It leaves the heart by the vessels called *arteries*, and returns to the heart by the vessels called *veins;* the terminations of the arteries and the commencements of the veins are, in the tissues, connected by the thin-walled microscopic vessels called *capillaries*. In the capillaries, leakage of the blood-plasma occurs; this exuded fluid (lymph) carries nutriment from the blood to the tissue-elements, and removes from them the waste products of their activity. The lymph is collected by lymphatic vessels, which converge to the main lymphatic, called the *thoracic duct*. This opens into the large veins near to their entrance into the heart; and thus the lymph is returned to the blood.

But blood is also a carrier of oxygen, and it is the pigment hæmoglobin which is the oxygen carrier; in the lungs the hæmoglobin combines with the oxygen of the air, and forms a loose compound of a bright scarlet colour called *oxyhæmoglobin*. This arterial or oxygenated blood is taken to the heart and thence propelled by the arteries all over the body, where the tissues take the respiratory oxygen from the hæmoglobin, and this removal of oxygen changes the colour of blood to the bluish-red tint it has in the veins. The veins take the blood *minus* a large quantity of oxygen and *plus* a large quantity of carbonic acid received in exchange from the tissues to the heart, which sends it to the lungs to get rid of its surplus carbonic acid, and replenish its store of oxygen; then the same round begins over again.

CHAPTER VI

MUSCULAR TISSUE

Muscle is popularly known as flesh. It possesses the power of contraction, and is, in the higher animals, the tissue by which their movements are executed. The muscles may be divided from a physiological standpoint into two great classes, the *voluntary* muscles, those which are under the control of the will, and the *involuntary* muscles, those which are not. The contraction of the involuntary muscles is, however, controlled by the nervous system, only by a different part of the nervous system from that which controls the activity of the voluntary muscles.

When muscular tissue is examined with the microscope, it is seen to be made up of small, elongated, thread-like structures, which are called *muscular fibres;* these are bound into bundles by connective tissue, and in the involuntary muscles there is in addition a certain amount of cement substance, stainable by nitrate of silver, between the fibres.

The muscular fibres are not all alike; those of the voluntary muscles are seen by the microscope to be marked by alternate dark and light stripings or striations; these are called *transversely striated muscular fibres.* The involuntary fibres have not got these markings as a rule. There is one important exception to this rule, namely, in the case of the heart, the muscular fibres of which are involuntary, but transversely striated. There are, however, histological differences between cardiac muscle and the ordinary voluntary striated muscles. The unstriated involuntary muscular fibres found in the walls of the stomach, intestine, bladder, blood-vessels, uterus, and other contractile organs are generally spoken of as *plain muscular fibres.*

From the histological standpoint there are, therefore, three varieties of muscular fibres found in the body of the higher animals: two of them are transversely striated, and one is not. The relationship of this histological classification to the physiological classification into voluntary and involuntary is shown in the following table:—

1. Transversely striated muscular fibres :	
a. In skeletal muscle . . .	VOLUNTARY.
b. In cardiac muscle . . .	INVOLUNTARY.
2. Plain muscular fibres :	
In blood-vessels, intestine, uterus, bladder, etc. . . .	

All kinds of muscular tissue are therefore composed of fibres, but the fibres are essentially different from those we have hitherto studied in the connective tissues. There, it will be remembered, the fibres are developed between the cells; here, in muscle, the fibres are developed from the cells; that is, the cells themselves become elongated to form the muscular fibres.

Voluntary Muscle.

The voluntary muscles are those which are sometimes called *skeletal*, constituting the whole of the muscular apparatus attached to the bones.*

Each muscle is enclosed in a sheath of areolar tissue, called the *Epimysium ;* this sends in partitions, or septa, dividing off the fibres into *fasciculi*, or bundles; the sheath of each bundle may be called the *Perimysium*. Between the individual fibres is a small amount of loose areolar tissue, called the *Endomysium*. The blood-vessels and nerves for the muscle are distributed in this areolar tissue.

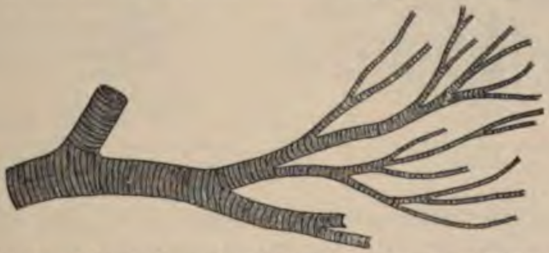

FIG. 102.—A branched muscular fibre from the frog's tongue. (Kölliker.)

The fibres vary in thickness and length a good deal, but they average $\frac{1}{500}$ inch in diameter, and about 1 inch in length. Each fibre is cylindrical in shape, with rounded ends; many become prolonged into tendon bundles (fig. 111), by which the muscle is attached to bone. As a rule they are unbranched, but the muscle fibres of the face and tongue divide into numerous branches before being inserted to the under surface of the skin, or mucous membrane (fig. 102). The fibres in these situations are also finer than in the majority of the voluntary muscles.

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* The muscular fibres of the pharynx, part of the œsophagus, and of the muscles of the internal ear, though not under the control of the will, have the same structure as the voluntary muscular fibres.

Each fibre consists of a sheath, called the *sarcolemma*, enclosing a soft material called the *contractile substance*. The sarcolemma is homogeneous, elastic in nature, and especially tough in fish and amphibia. It may readily be demonstrated in a microscopic preparation of fresh muscular fibres by applying gentle pressure to the cover slip; the contractile substance is thereby ruptured, leaving the sarcolemma bridging the space (fig. 103). To the sarcolemma are seen adhering some nuclei.

The contractile substance within the sheath is made up of alternate discs of dark and light substance.

Muscular fibres contain oval nuclei. In mammalian muscle these are situated just beneath the sarcolemma; but in frog's muscle they occur also in the thickness of the muscular fibre. The chromoplasm of the nucleus has generally a spiral arrangement, and often there is a little granular protoplasm (well seen in the muscular fibres of the diaphragm) around each pole of the nucleus.

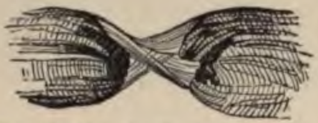

FIG. 103.—Muscular fibre torn across, the sarcolemma still connecting the two parts of the fibre. (Todd and Bowman.)

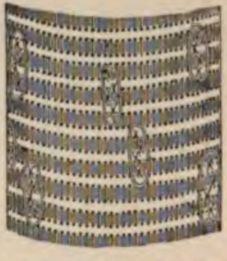

FIG. 104.—Muscular fibre of a mammal highly magnified. The surface of the fibre is accurately focussed. (Schäfer.)

The foregoing facts can be made out with a low power of the microscope; on examining muscular fibres with a high power other details can be seen. Treatment with different reagents brings out still further points of structure. These are differently described and differently interpreted by different histologists; and perhaps no subject in the whole of microscopic anatomy has been more keenly debated than the structure of a muscular fibre, and the meaning of the changes that occur when it contracts. A good deal of the difficulty has doubtless arisen from the fact that a muscular fibre is cylindrical, and if one focusses the surface one gets different optical effects from those obtained by focussing deep in the substance of the fibre. I shall, in the following account of the structure of striated muscle, adhere very closely to the writings of Professor Schäfer.

If the surface is carefully focussed rows of apparent granules are seen lying at the boundaries of the light streaks, and fine longitudinal lines passing through the dark streaks may be detected uniting the apparent granules (fig. 104).

In specimens treated with dilute acids or gold chloride, the granules are seen to be connected side by side, or transversely also. This reticulum (fig. 105), with its longitudinal and transverse meshes, was at one time considered to be the essential contractile portion of the muscular fibre; it was thought that on contraction the transverse networks, with their enlargements, the granules, became increased by the longitudinal strands diminishing in length and running into them. Most histologists have rejected this idea, and regard the network as mere interstitial substance lying between the essentially contractile portions of the muscle. A muscular fibre is thus made up of what are variously called *fibrils, muscle-columns* or *sarcostyles;* and the longitudinal interstitial substance with cross networks comprising the reticulum just referred to is called *sarcoplasm.* By the use of certain reagents, such as osmic acid or alcohol, the muscle-columns or sarcostyles may be completely separated from one another.

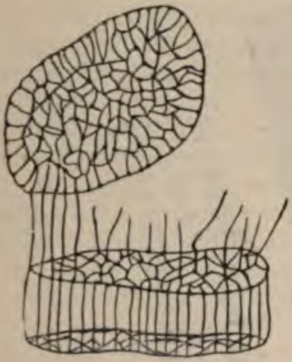

FIG. 105.—Portion of muscle-fibre of water-beetle, showing network very plainly. One of the transverse networks is split off, and some of the longitudinal bars are shown broken off. (After Melland.)

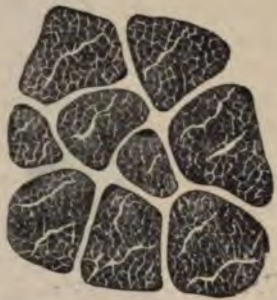

FIG. 106.—Transverse section through muscular fibres of human tongue. The nuclei are deeply stained, situated at the inside of the sarcolemma. Each muscle fibre shows "Cohnheim's areas." × 450. (Klein and Noble Smith.)

A transverse section of a muscular fibre (fig. 106) shows the sections of these sarcostyles; the interstitial sarcoplasm is represented as white in the drawing. The angular fields separated by sarcoplasm may still be called by their old name, *areas of Cohnheim.*

If, instead of focussing the surface of a fibre, it is observed in its depth, a fine dotted line is seen bisecting each light stripe; this has been variously termed *Dobie's line*, or *Krause's membrane* (fig. 107). At one time this was believed to be an actual membrane continuous with the sarcolemma. It is probably very largely an optical effect, caused by light being transmitted between discs of different refrangibility.

If cross membranes do exist they are not very resistant; this was well shown by an accidental observation first made by Kühne, and subsequently seen by others. A minute thread-worm, called the ***Myorectes***, was observed crawling up the interior of the contractile substance of a muscular fibre; it crawled without any opposition from membranes, and the track it left, closed up slowly behind it without interfering with the normal cross-striations of the contractile substance. This observation strikingly illustrates the fact that the contractile substance in a muscular fibre is fluid, but only semi-fluid, for the closing of the thread-worm's track occurred slowly as a hole always closes in a viscous material.

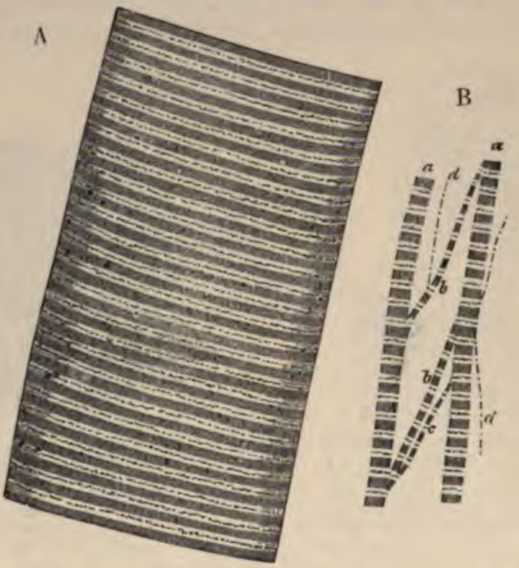

FIG. 107.—A. Portion of a human muscular fibre. × 800. B. Separated bundles of fibrils equally magnified; *a*, *a*, larger, and *b*, *b*, smaller collections; *c*, still smaller; *d*, *d*, the smallest which could be detached, possibly representing a single series of sarcous elements. (Sharpey.)

Another appearance which is sometimes seen is a fine clear line running across the fibre in the middle of each dark band. It is called *Hensen's line* or *disc*.

A muscular fibre may not only be broken up into fibrils or muscle-columns, but under the influence of some reagents like dilute hydrochloric acid, it can be broken up into discs, the cleavage occurring in the centre of each light stripe. Bowman, the earliest to study muscular fibres with profitable results, concluded that the subdivision of a fibre into fibrils was a phenomenon of the same kind as the cross cleavage into discs. He considered that both were artificially produced by a separation in one or the other direction of particles of the fibre he called "sarcous elements." The cleavage into discs is however much rarer than the separation into fibrils; indeed, indications of the fibrils are seen in perfectly fresh muscle before any reagent has been added, and this is markedly evident in the wing muscles of many insects. It is now believed that a muscular fibre is built up of contiguous fibrils or sarcostyles, while cleavage into discs is a purely artificial phenomenon.

Haycraft, who has also investigated the question of muscular structure, concludes that the cross striation is entirely due to optical phenomena. The sarcostyles are varicose, and where they are enlarged different refractive effects will be produced from those caused by the intermediate narrow portions. This view he has very ingeniously supported by taking negative casts of muscular fibres by pressing them on to the surface of collodion films. The collodion cast shows alternate dark and light bands like the muscular fibres.

Schäfer is unable to accept this view; he regards the substance of the sarcostyle in its dark stripes as being of different composition, and not merely of different diameter, from the sarcostyle in the region of the light stripes; it certainly stains very differently with many reagents, especially chloride of gold. His views regarding the intimate structure of a sarcostyle have been worked out chiefly in the wing muscles of insects, where the sarcostyles are separated by a considerable quantity of interstitial sarcoplasm, and a brief summary of his conclusions is as follows:—

Each sarcostyle is subdivided in the middle of each light stripe by transverse lines (membranes of Krause) into successive portions, which may be termed *sarcomeres*. Each sarcomere is occupied by a portion of the dark stripe of the whole fibre; this portion of the dark stripe may be called a *sarcous element*.* The sarcous element is really double, and in the stretched fibre (fig. 108, B) separates into two at the line of Hensen. At either end of the sarcous element is a clear interval separating it from Krause's membrane; this clear interval is more evident in the extended sarcomere (fig. 108, B), but diminishes on contraction (fig. 108, A). The cause of this is to be found in the structure of the sarcous element. It is pervaded with longitudinal canals or pores open towards Krause's membrane, but closed at Hensen's line. In the contracted muscle the clear part of the muscle substance passes into these pores, disappears from view to a great extent, swells up the sarcous element, widens it and shortens the sarcomere. In the extended muscle, on the other hand, the clear substance passes out from the pores of the sarcous element, and lies between it and the membrane of Krause; this lengthens and narrows the sarcomere.* This is shown in the diagrams. It may be added that the sarcous element does not lie free in the middle of the sarcomere, but is attached at the sides to a fine enclosing envelope, and at either end to Krause's membrane by fine lines running through the clear substance (fig. 109, A).

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* Notice that this expression has a different meaning from what it originally had when used by Bowman.

This view is interesting, because it brings into harmony amœboid, ciliary, and muscular movement. In all three instances we have protoplasm composed of two materials, spongioplasm and hyaloplasm. In amœboid movement the irregular arrangement of the spongioplasm allows the hyaloplasm to flow in and out of it in any direction. In ciliary movement the flow is limited by the arrangement of the spongioplasm to one direction; hence the limitation of the movement in one direction (see p. 30). In muscle, also, the definite arrangement of the spongioplasm (represented by the sarcous element) in a longitudinal direction limits the movement of the hyaloplasm (represented by the clear substance of the light stripe), so that it must flow either in or out in that particular direction. The muscular fibre is made up of sarcostyles and the sarcostyle of sarcomeres. The contraction of

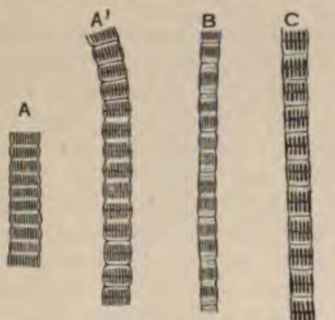

FIG. 108.—Sarcostyles from the wing-muscles of a wasp.

A, A'. Sarcostyles showing degrees of contraction.

B. A sarcostyle extended with the sarcous elements separated into two parts.

C. Sarcostyles moderately extended (semidiagrammatic). (E. A. Schäfer.)

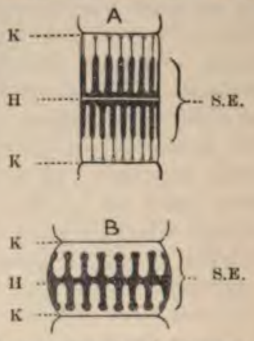

FIG. 109.—Diagram of a sarcomere in a moderately extended condition, A, and in a contracted condition, B.

K, K, Krause's membranes; H, plane of Hensen; S.E., poriferous sarcous element. (E. A. Schäfer.)

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* The existence of open pores is not admitted by all observers. These regard the passage of fluid in and out of the sarcous element as due to diffusion through its membrane.

the whole muscle is only the sum total of the contraction of all the constituent sarcomeres.

In an ordinary muscular fibre it is stated that when it contracts, not only does it become thicker and shorter, but the light stripes become dark and the dark stripes light. This again is only an optical illusion, and is produced by the alterations in the shape of the sarcostyles, affecting the sarcoplasm that lies between them. When the sarcous elements swell during contraction, the sarcoplasm accumulates opposite the membranes of Krause, and diminishes in amount opposite the sarcous elements; the accumulation of sarcoplasm in the previously light stripes makes them appear darker by contrast than the dark stripes proper. This is very well shown in fig. 110. There is no true reversal of the stripings in the sarcostyles themselves.

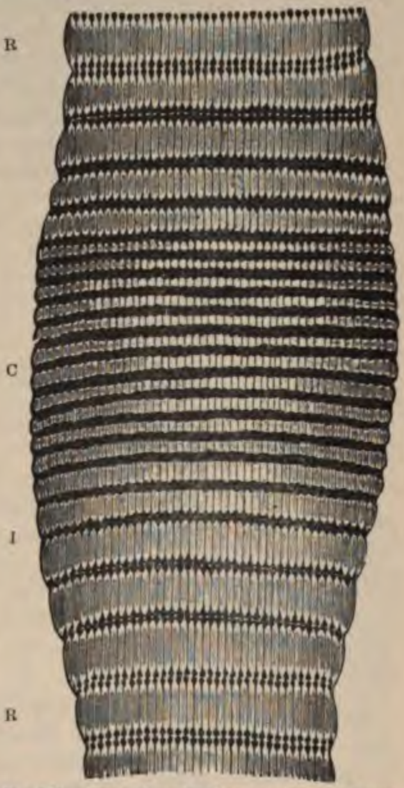

FIG. 110.—Wave of contraction passing over a muscular fibre of water-beetle. R, R, portions of the fibre at rest; C, contracted part; I, I, intermediate condition. (Schäfer.)

That this is the case can be seen very well when a muscular fibre is examined with polarised light. A polarising microscope contains a Nicol's prism beneath the stage of the microscope which polarises the light passing through the object placed on the stage. The eye-piece contains another Nicol's prism, which detects this fact. If the two Nicols are parallel, the light passing through the first passes also through the second; but if the second is at right angles to the first, the light cannot traverse it and the field appears dark. If an object on the microscope stage is doubly refracting it will appear bright in this dark field; if it remains dark it is singly refracting. The sarcoplasm is singly refracting or isotropous; it remains dark in the dark field of the polarising microscope. The muscle columns or sarcostyles are in great measure doubly refracting or anisotropous, and appear bright in the dark field of the polarising microscope. The sarcostyle, however, is not wholly doubly refracting; the sarcous elements are doubly refracting, and the clear intervals are singly refracting. On contraction there is no reversal of these appearances, though of course the relative thickness of the singly refracting intervals varies inversely with that of the doubly refracting sarcous elements.

Ending of Muscle in Tendon.—A tendon-bundle passes to each muscular fibre, and becomes firmly united to the sarcolemma. The areolar tissue between the tendon-bundles becomes also continuous with that between the muscular fibres (fig. 111).

Blood-vessels of Muscle.—The arteries break up into capillaries, which run longitudinally in the endomysium, transverse branches connecting them (fig. 112). No blood-vessels ever penetrate the sarcolemma. The muscular fibres are thus, like other tissues, nourished by the exudation from the blood called *lymph*. The lymph is removed by lymphatic vessels found in the perimysium.

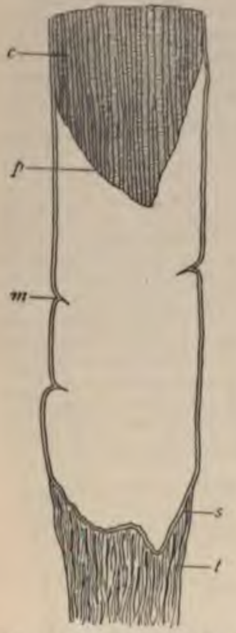

FIG. 111.—Termination of a muscular fibre in a tendon-bundle. *m*, sarcolemma; *s*, the same passing over the end of bundle; *p*. extremity of muscular substance *c*, retracted from the end of sarcolemma tube; *t*, tendon bundle fixed to sarcolemma. (Ranvier.)

The nerves of voluntary muscle pierce the sarcolemma, and terminate in expansions called *end-plates*, to be described on p. 95.

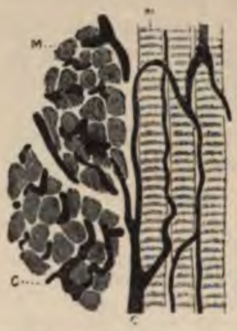

FIG. 112.—Three muscular fibres running longitudinally, and two bundles of fibres in transverse section, M, from the tongue. The capillaries, C, are injected. × 150. (Klein and Noble Smith.)

Neuro-muscular Spindles.—Bundles of fine muscular fibres enclosed within a thick lamellated sheath of connective tissue are found scattered through voluntary muscles; they are especially numerous near the tendons and in the proximity of intra-muscular septa. It is remarkable that they have not been found in the ocular or tongue muscles. These structures are called *neuro-muscular spindles;* they vary in length from $\frac{1}{8}$ to $\frac{1}{3}$ inch, and are about $\frac{1}{125}$ inch in diameter. Each receives a nerve fibre which divides into secondary and tertiary branches. The myelin sheath is lost, and the tertiary branches encircle the muscular fibres, breaking up usually into a network. It is believed that these are sensory end organs in the muscle. (See further, chapter on Touch.)

Red Muscles.

In many animals, such as the rabbit, and some fishes, most of the muscles are pale, but some few (like the diaphragm, crureus, soleus, semi-membranosus in the rabbit) are red. These muscles contract more slowly than the pale muscles, and their red tint is due to hæmoglobin contained within their contractile substance.

In addition to these physiological distinctions, there are histological differences between them and ordinary striped muscle. These histological differences are the following:—

1. Their muscular fibres are thinner.
2. They have more sarcoplasm.
3. Longitudinal striation is therefore more distinct.
4. Transverse striation is more irregular than usual.
5. Their nuclei are situated not only under the sarcolemma, but also in the thickness of the fibre.
6. The transverse loops of the capillary network are dilated into little reservoirs, far beyond the size of ordinary capillaries.

Cardiac Muscle.

The muscular fibres of the heart, unlike those of most of the involuntary muscles, are striated; but although, in this respect, they resemble the skeletal muscles, they have distinguishing characteristics of their own. The fibres which lie side by side are united at frequent intervals by short branches (fig. 113). The fibres are smaller than those of the ordinary striated muscles, and their transverse striation is less distinct. No sarcolemma can be discerned. Each fibre has only one nucleus which is situated in the middle of its substance. At the junctions of the fibres there is a certain amount of cementing material, stainable by silver nitrate. This is bridged across by fine fibrils from cell to cell.

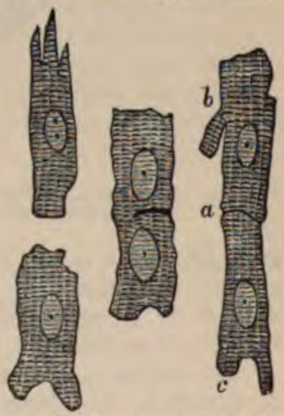

FIG. 113.—Muscular fibre-cells from the heart. (E. A. Schäfer.)

Plain Muscle.

Plain muscle forms the proper muscular coats (1.) of the digestive canal from the middle of the œsophagus to the internal sphincter ani; (2.) of the ureters and urinary bladder; (3.) of the trachea and bronchi; (4.) of the ducts of glands; (5.) of the gall-bladder; (6.) of the vesiculæ seminales; (7.) of the uterus and Fallopian tubes; (8) of blood-vessels and lymphatics; (9.) of the iris, and ciliary muscle of the eye. This form of tissue also enters largely into the composition (10.) of the *tunica dartos*, the contraction of which is the principal cause of the wrinkling and contraction of the scrotum on exposure to cold. It occurs also in the skin generally, being found surrounding the secreting part of the sweat glands and in small bundles attached to the hair follicles; it also occurs in the areola of the nipple. It is composed of long, fusiform cells (fig. 114), which vary in length, but are not as a rule more than $\frac{1}{500}$ inch long. Each cell has an oval or rod-shaped nucleus. The cell substance is longitudinally but not transversely striated. Each cell or fibre, as it may also be termed, has a delicate sheath. The fibres are united by cementing material, which can be stained by silver nitrate. This intercellular substance is bridged across by fine filaments passing from cell to cell.

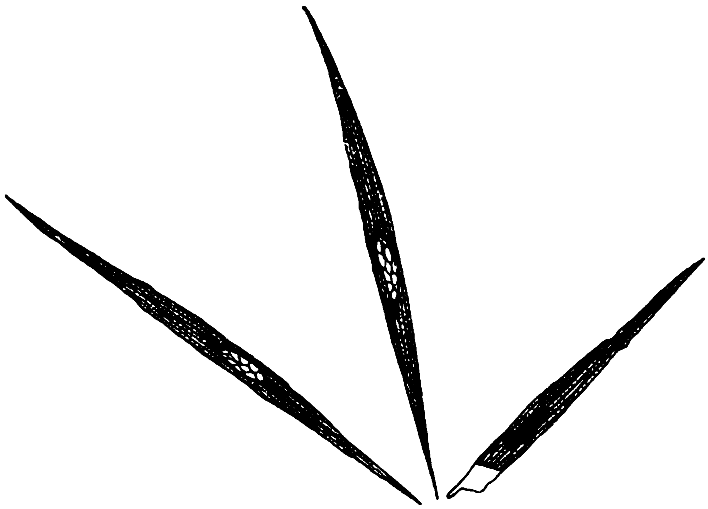

FIG. 114.—Muscular fibre-cells from the muscular coat of intestine—highly magnified. Note the longitudinal striation, and in the broken fibre the sheath is visible.

The nerves in involuntary muscle (both cardiac and plain) do not terminate in end-plates, but by plexuses or networks, which ramify between and around the muscular fibres.

Development of Muscular Fibres.

All muscular fibres (except those of the sweat glands which are epiblastic) originate from the mesoblast. The *plain fibres* are simply elongated cells in which the nucleus becomes rod-shaped. In *cardiac* muscle, the likeness to the original cells from which the fibres are formed is not altogether lost, and in certain situations (immediately beneath the lining membrane of the ventricles) there are found peculiar fibres called after their discoverer *Purkinje's fibres*; these are large clear quadrangular cells with granular protoplasm containing several nuclei in the centre, and striated at the margin. It appears that the differentiation of these cells is arrested at an early stage, though they continue to grow in size.

Voluntary muscular fibres are developed from cells which become elongated, and the nuclei of which multiply. In most striated muscle fibres the nuclei ultimately take up a position beneath the cell-wall or sarcolemma which is formed on the surface. Striations appear first along one side, and extend round the fibre (fig. 115), then they extend into the centre.

During life new fibres appear to be formed in part by a longitudinal splitting of pre-existing fibres; this is preceded by a multiplication of nuclei; and in part by the lengthening and differentiation of embryonic cells (sarcoplasts) found between the fully formed fibres.

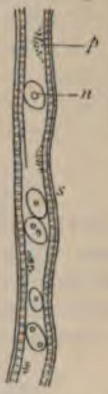

FIG. 115.—Developing muscular fibre from fœtus of two months. (Ranvier).

In plain muscle, growth occurs in a similar way: this is well illustrated in the enlargement of the uterus during pregnancy; this is due in part to the growth of the pre-existing fibres, and in part to the formation of new fibres from small granular cells lying between them. After parturition the fibres shrink to their original size, but many undergo fatty degeneration and are removed by absorption.

CHAPTER VII

NERVE

NERVOUS tissue is the material of which the nervous system is composed. The nervous system is composed of two parts, the ***central nervous system***, and the ***peripheral nervous system***. The central nervous system consists of the brain and spinal cord; the peripheral nervous system consists of the nerves, which conduct the impulses to and from the central nervous system, and thus bring the nerve centres into relationship with other parts of the body.

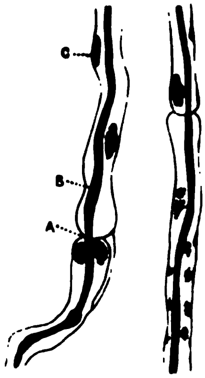

FIG. 116.—Two nerve-fibres of sciatic nerve. A. Node of Ranvier. B. Axis-cylinder. C. Sheath of Schwann, with nuclei. Medullary sheath is not stained. × 800. (Klein and Noble Smith.)

FIG. 117.—Axis cylinder, highly magnified, showing its component fibrils. (M. Schultze.)

Some of the nerves conduct impulses from the nerve-centres and are called ***efferent***; those which conduct impulses in the opposite direction are called ***afferent***. When one wishes to move the hand, the nervous impulse starts in the brain and passes down the efferent or motor nerve-tracts to the muscles of the hand, which contract; when one feels pain in the hand, afferent or sensory nerve-tracts convey an impulse to the brain which is there interpreted as a sensation. If all the nerves going to the hand are cut through, all communication with the nerve-centres is destroyed, and the hand loses the power of moving under the influence of the will, and the brain receives no impulses from the hand, or, as we say, the hand has lost sensibility.

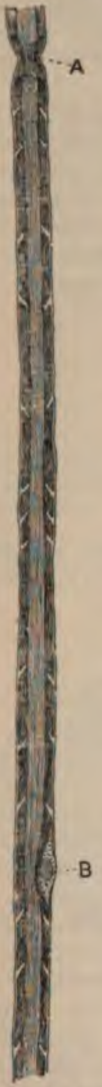

FIG. 118. — Nerve-fibre stained with osmic acid. A, node; B, nucleus. (Key and Retzius.)

This distinction between efferent and afferent nerves is a physiological one, which we shall work out more thoroughly later on. No histological distinction can be made out between motor and sensory nerves, and it is histological structure which we wish to dwell upon in this chapter.

Under the microscope nervous tissue is found to consist essentially of *nerve-cells* and their branches. The nerve-cells are contained in the brain and spinal cord, and in smaller collections of cells on the course of the nerves called *ganglia*. The part of the nerve-centres containing cells is called *grey matter*.

Long branches of the nerve-cells are known as *nerve-fibres*. These become sheathed in a manner to be immediately described, and are contained in the nerves, and in the *white matter* of brain and spinal cord. The bodies of nerve-cells differ in size, shape, and arrangement, and we shall discuss these fully when we get to the nerve-centres. For the present it will be convenient to confine ourselves to the nerve-fibres as they are found in a nerve.

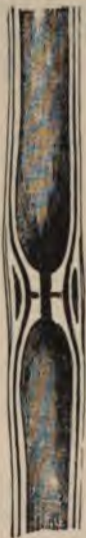

FIG. 119.—A node of Ranvier in a medullated nerve-fibre, viewed from above. The medullary sheath is interrupted, and the primitive sheath thickened. Copied from Axel Key and Retzius. × 750. (Klein and Noble Smith.)

Nerve-fibres are of two histological kinds, *medullated* and *non-medullated*. Medullated nerve-fibres are found in the white matter of the nerve-centres and in the nerves originating from the brain and spinal cord. Non-medullated nerve-fibres occur in the sympathetic nerves.

The **medullated** or **white fibres** are characterised by a sheath of white colour, fatty in nature, and stained black by osmic acid; it is called the ***medullary sheath*** or ***white substance of Schwann;*** this sheathes the essential part of the fibre which is a process from a nerve-cell, and is called the ***axis cylinder.*** Outside the medullary sheath is a thin homogeneous membrane of elastic nature called the ***primitive sheath*** or ***neurilemma.***

The axis cylinder is a soft transparent thread in the middle of the fibre; it is made up of exceedingly fine fibrils (fig. 117) which stain readily with gold chloride. ***The medullary sheath*** gives a characteristic double contour and tubular appearance to the fibre. It is interrupted at regular intervals known as the ***nodes of Ranvier.*** The stretch of nerve between two nodes is called an ***inter-node,*** and in the middle of each inter-node is a nucleus which belongs to the primitive sheath. Besides these interruptions, a variable number of oblique clefts are also seen dividing the sheath into ***medullary segments*** (fig. 118); but most if not all of these are produced artificially in the preparation of the specimen.

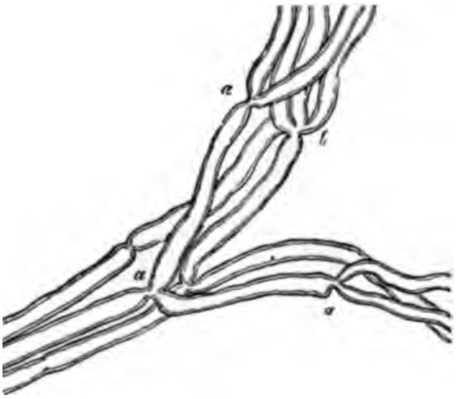

Fig. 120.—Small branch of a muscular nerve of the frog, near its termination, showing division of the fibres. *a*, into two; *b*, into three. × 350. (Kölliker.)

The medullary sheath also contains a horny substance called ***neurokeratin:*** the arrangement of this substance is in the form of a network or reticulum holding the fatty matter of the sheath in its meshes. The occurrence of horny matter in the epidermis, in the development of the enamel of teeth and in nerve is an interesting chemical reminder that all these tissues originate from the same embryonic layer, the epiblast. The fatty matter consists largely of *lecithin*, a phosphorised fat, and *cholesterin*, a monatomic alcohol.

Near their terminations the nerve-fibres branch: the branching occurs at a node (fig. 120).

Staining with silver nitrate produces a peculiar appearance at the nodes, forming what is known as the *crosses of Ranvier*.

One limb of the cross is produced by the dark staining of cement substance which occurs between the segments of the neurilemma; the other limb of the cross is due to the staining of a number of minute transverse bands in the axis cylinder (*Fromann's lines*), which is here not closely invested by the medullary sheath (fig. 121).

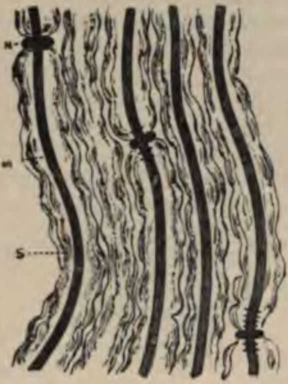

FIG. 121.—Several fibres of a bundle of medullated nerve-fibres acted upon by silver nitrate to show behaviour of nodes of Ranvier, M, towards this reagent. The silver has penetrated at the nodes, and has stained the axis-cylinder, M, for a short distance. S, the white substance. (Klein and Noble Smith.)

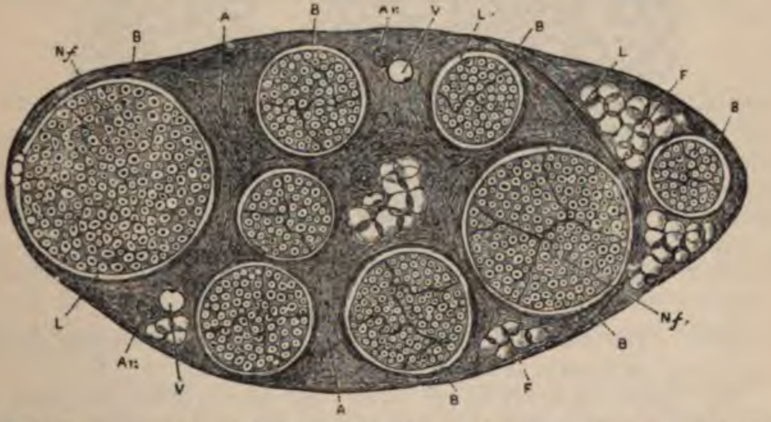

FIG. 122.—Transverse section of the sciatic nerve of a cat about × 100.—It consists of bundles (*funiculi*) of nerve-fibres ensheathed in a fibrous supporting capsule, *epineurium*, A; each bundle has a special sheath (not sufficiently marked out from the *epineurium* in the figure) or *perineurium* B; the nerve-fibres N *f* are separated from one another by *endoneurium*; L, lymph spaces; Ar, artery; V, vein; F, fat. Somewhat diagrammatic. (V. D. Harris.)

The arrangement of the nerve-fibres in a nerve is best seen in a transverse section.

The nerve is composed of a number of bundles or *funiculi* of nerve-fibres bound together by connective tissue. The sheath of the whole nerve is called the *epineurium;* that of the funiculi the *perineurium;* that which passes between the fibres in a funiculus, the *endoneurium* (fig. 122). Single nerve-fibres passing to their destination are surrounded by a prolongation of the perineurium, known as the *Sheath of Henle.* The nerve trunks themselves receive nerve-fibres which ramify and terminate as end-bulbs in the epineurium.

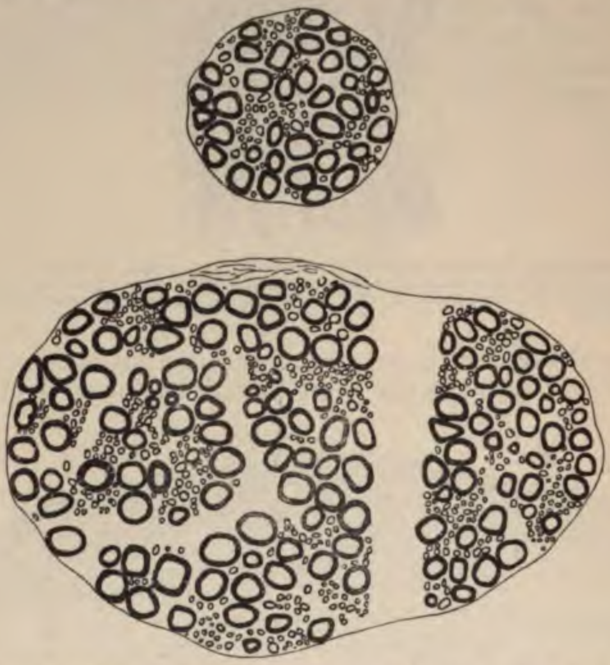

FIG. 123.—Section across the second thoracic anterior root of the dog, stained with osmic acid. (Gaskell.)

The size of the nerve-fibres varies; the largest fibres are found in the spinal nerves, where they are 14·4 to 19μ in diameter.* Others mixed with these measure 1·8 to 3·6μ. These small nerve-fibres are the visceral nerves; they pass to collections of nerve-cells called the sympathetic ganglia, whence they emerge as non-medullated fibres, and are distributed to involuntary muscle. They are well seen in sections stained by osmic acid, the black rings being the stained medullary sheaths (fig. 123).

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* μ = micro-millimetre = $\frac{1}{1000}$ millimetre.

The non-medullated fibres or *fibres of Remak* have no medullary sheath, and are therefore devoid of the double contour of the medullated fibres, and are unaffected in appearance by osmic acid. They consist of an axis cylinder covered by a nucleated fibrillated sheath. They branch frequently.

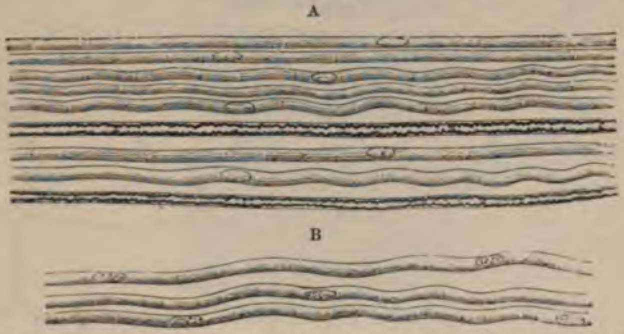

FIG. 124.—Grey, or non-medullated nerve-fibres. A. From a branch of the olfactory nerve of the sheep; two dark-bordered or white fibres from the fifth pair are associated with the pale olfactory fibres. B. From the sympathetic nerve. × 450. (Max Schultze.)

Though principally found in the sympathetic nerves, a few are found in the spinal nerves mixed with the medullated fibres.

Termination of Nerves in Muscle.

In the *voluntary muscles* the motor nerve-fibres have special end organs called *end-plates.* The fibre branches two or three times (figs. 120, 125), and each branch goes to a muscular fibre. Here the neurilemma becomes continuous with the sarcolemma, the medullary sheath stops short, and the axis cylinder branches repeatedly. This ramification is embedded in a layer of granular protoplasm containing numerous nuclei. Considerable variation in shape of the end-plates occurs in different parts of the animal kingdom. Somewhat similar nerve-endings are seen in tendon; these, however, are doubtless sensory (figs. 126, 127).

In the *involuntary muscles*, the fibres which are for the most part non-medullated form complicated plexuses near their termination. The plexus of Auerbach (fig. 128) between the muscular coats of the intestine is a typical case. Groups of nerve-cells will be noticed at the junctions of the fine nervous cords. From these plexuses fine branches pass off and bifurcate at frequent intervals, until at last ultimate fibrillæ are reached. These subdivisions of the axis cylinders do not anastomose with one another, but they come into close relationship with the involuntary muscular fibres; though some histologists have stated that they end in the nuclei of the muscular fibres, it is now believed that they do not pass into their interior.

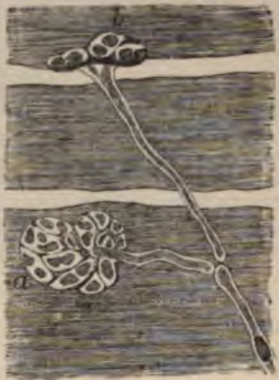

FIG. 125.—From a preparation of the nerve-termination in the muscular fibres of a snake. *a*, End-plate seen in surface view. *b*, End-plate seen in profile. (Lingard and Klein.)

The terminations of sensory nerves are in some cases plexuses, in others special end organs. We shall deal with these in our study of sensation.

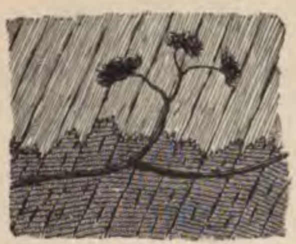

FIG. 126.—Termination of medullated nerve-fibres in tendon near the muscular insertion. (Golgi.)

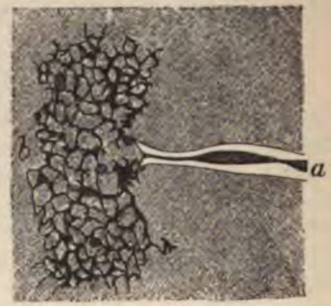

FIG. 127.—One of the reticulated end-plates of fig. 126, more highly magnified. *a*, medullated nerve-fibres; *b*, reticulated end-plates. (Golgi.)

Development of Nerve-fibres.

A nerve-fibre is primarily an out-growth from a nerve-cell, as is shown in the accompanying diagram. A nerve-cell, though it may have many branches, only gives off one process which becomes the axis cylinder of a nerve-fibre. This acquires a medullary sheath when it passes into the white matter of the brain or spinal cord, and a primitive sheath when it leaves the nerve-centre and gets into the nerve. But at first the axis cylinder is not sheathed at all.

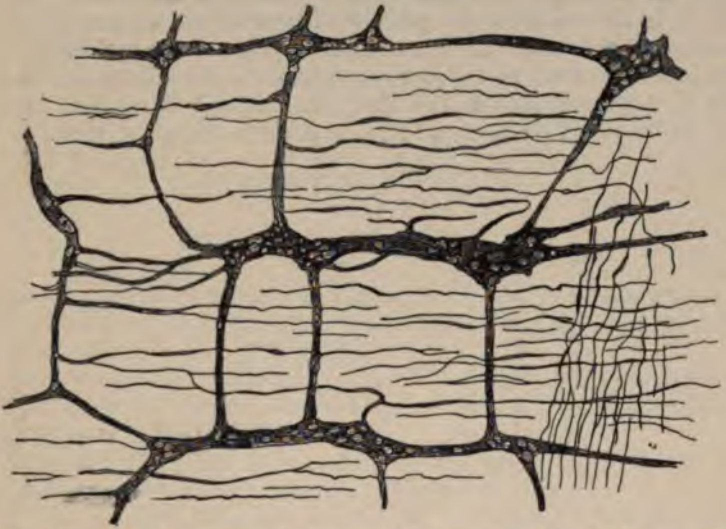

FIG. 128.—Plexus of Auerbach, between the two layers of the muscular coat of the intestine. (Cadiat.)

The formation of the sheaths is still a matter of doubt, but the generally accepted opinion is that the primitive sheath is formed by cells which become flattened out and wrapped round the fibre end to end. These are separated at the nodes by intercellular or cement substance stainable by silver nitrate (fig. 121). These cells are

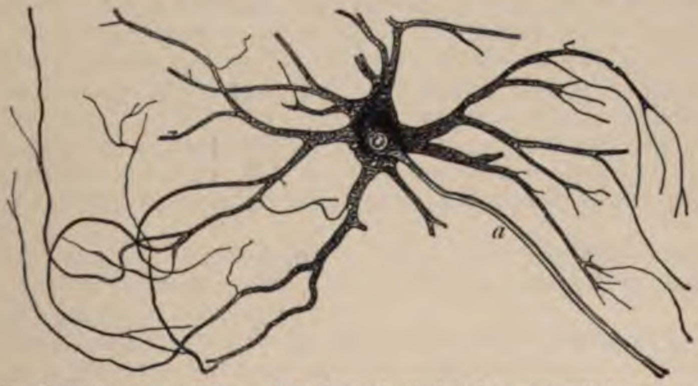

FIG. 129.—Multipolar nerve-cell from anterior horn of spinal cord; *a*, axis cylinder process. (Max Schultze.)

probably mesoblastic. The medullary sheath is formed, according to some, by a fatty change occurring in the parts of these same cells which are nearest to the axis cylinder, but it is much more probable that it is formed from the peripheral layer of the axis cylinder; the presence of neurokeratin in it distinctly points to an epiblastic origin. The fact also that, in the nerve centres, the medullated nerve-fibres have no primitive sheath, and the phenomena of Wallerian degeneration, to be described later, all tend to confirm the same view.

CHAPTER VIII

IRRITABILITY AND CONTRACTILITY

Irritability or **Excitability** is the power that certain tissues possess of responding by some change to the action of an external agent. This external agent is called a **stimulus**.

Undifferentiated cells like white blood-corpuscles are irritable; when stimuli are applied to them they execute the movements we have learnt to call amœboid.

Ciliated epithelium cells and muscular fibres are irritable; they also execute movements under the influence of stimuli.

Nerves are irritable; when they are stimulated, a change is produced in them; this change is propagated along the nerve, and is called a nervous impulse; there is no change of form in the nerve visible to the highest powers of the microscope; much more delicate and sensitive instruments than a microscope must be employed to obtain evidence of a change in the nerve; it is of a molecular nature. But the irritability of nerve is readily manifested by the results the nervous impulse produces in the organ to which it goes; thus the stimulation of a motor nerve produces a nervous impulse in that nerve which, when it reaches a muscle, causes the muscle to contract: stimulation of a sensory nerve produces a nervous impulse in that nerve which, when it reaches the brain, causes a sensation.

Secreting glands are irritable; when irritated or stimulated they secrete.

The electrical organs found in many fishes like the electric eel, and torpedo ray, are irritable; when they are stimulated they give rise to an electrical discharge.

Contractility is the power that certain tissues possess of responding to a stimulus by change of form. Contractility and irritability do not necessarily go together; thus both muscle and nerve are irritable, but of the two, only muscle is contractile.

Some movements visible to the microscope are not due to contractility; thus granules in protoplasm or in a vacuole may often be seen to exhibit irregular, shaking movements due simply to vibrations transmitted to them from the outside. Such movement is known as *Brownian movement.*

Instances of contractility are seen in the following cases:—

1. The movements of protoplasm seen in simple animal and vegetable cells; in the former we have already considered streaming, gliding, and amœboid movement (see p. 12); in the latter case we have noted the rotatory movements of the protoplasm within the cell wall in certain plants (see p. 13).

2. The movements of pigment cells. These are well seen under the skin of such an animal as the frog; under the influence of electricity and of other stimuli, especially of light, the pigment granules are massed together in the body of the cell, leaving the processes quite transparent (fig. 130). If the stimulus is removed the granules gradually extend into the processes again. Thus the skin of the frog is sometimes uniformly dusky, and sometimes quite light coloured. The chamæleon is an animal which has become almost proverbial, since it possesses the same power to a marked degree. This function is a protective one; the animal approximates in colour that of its surroundings, and so escapes detection.

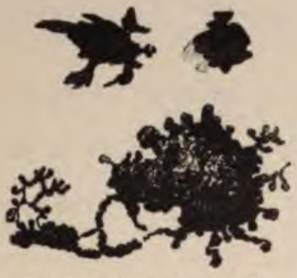

FIG. 130.—Frog's pigment cells.

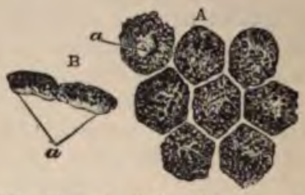

FIG. 131.—Pigment cells from the retina. A, cells still cohering, seen on their surface; *a*, nucleus indistinctly seen. In the other cells the nucleus is concealed by the pigment granules. B, two cells seen in profile; *a*, the outer or posterior part containing scarcely any pigment. × 370. (Henle.)

In the retina we shall find a layer of pigment cells (fig. 131), the granules in which are capable of moving in the protoplasm in a somewhat similar way; the normal stimulus here also is light.

3. Ciliary movement; here we have a much more orderly movement which has already been described (see p. 29).

4. In Vorticellæ, a spiral thread of protoplasm in their stalk enables them by contracting it to lower the bell at the end of the stalk.

5. In certain of the higher plants, such as the sensitive and carnivorous plants, movements of the stalks and sensitive hairs of the leaves occur under the influence of stimuli.

6. Muscular movement. This for the student of human physiology is the most important of the series; it is by their muscles that

the higher animals (man included) execute the greater number of their movements.

If we contrast together amœboid, ciliary, and muscular movement, we find that they differ from each other very considerably. Amœboid movement can occur in any part of an amœboid cell, and in any direction. Ciliary and muscular movement are limited to one direction; but they are all essentially similar, consisting of the movement of hyaloplasm in and out of spongioplasm; it is the arrangement of the spongioplasm that limits and controls the movement of the hyaloplasm (see also p. 84).

Rhythmicality.—In some forms of movement there is not only order in direction, but order in time also. This is seen in ciliary movement, and in many involuntary forms of muscular tissue, such as that of the heart. Here periods of contraction alternate with periods of rest, and this occurs at regular intervals. Under the influence of certain saline solutions,* voluntary muscles may be made artificially to exhibit rhythmic contractions.

A familiar instance of rhythmic movement in the inorganic world is seen in a water-tap nearly turned off but dripping; water accumulates at the mouth of the tap till the drop is big enough to fall; it falls, and the process is repeated. If, instead of water, gum or treacle, or some other viscous substance is watched under similar circumstances, the drops fall much more slowly; each drop has to get bigger before it possesses enough energy to fall. Thus we may get different degrees or rates of rhythmic movement. So in the body, during the period of rest, the cilium or the heart is accumulating potential energy, till, as it were, it becomes so charged that it discharges; potential energy is converted into kinetic energy or movement.

When contraction travels as a wave along muscular fibres, or from one muscular fibre to another, the term *peristalsis* is employed. These waves are well seen in such a muscular tube as the intestine, and are instrumental in moving its contents along. The heart's contraction is a similar but more complicated peristalsis occurring in a rhythmic manner.

Muscle and nerve are admirable tissues for studying irritability and contractility.

The question may be first asked, what evidence there is of irritability in muscle? May not the irritability be a property of the nerve-fibres which are distributed throughout the muscle and terminate in its fibres? The doctrine of independent muscular irritability was enunciated by Haller more than a century ago, and was afterwards keenly debated. It was finally settled by an experiment of Claude Bernard which can be easily repeated by every student.

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* Biedermann's fluid has the following composition:—Sodium chloride 5 grammes, alkaline sodium phosphate 2 gr., sodium carbonate 0·5 gr., water 1 litre. If one end of the sartorius of a curarised frog is dipped into this fluid, it contracts rhythmically in a manner analogous to the heart.

If a frog is taken and its brain destroyed by pithing, it loses consciousness, but the circulation goes on, and the tissues of its body retain their vitality for a considerable time. If now a few drops of a solution of *curare*, the Indian arrow poison, are injected with a small syringe under the skin of its back, it loses in a few minutes all power of movement. If next the sciatic or any other nerve going to muscle is dissected out and stimulated, no movement occurs in the muscles to which it is distributed. Curare paralyses the motor end-plates, so that for all practical purposes the muscles are nerveless; or rather nervous impulses cannot get past the end-plates and cause any effect on the muscles. But if the muscles are stimulated themselves they contract.

Another proof that muscle possesses inherent irritability was adduced by Kühne. In part of some of the frog's muscles (*e.g.* part of the sartorius) there are no nerves at all; yet they are irritable and contract when stimulated.

The evidence of the statement just made that the poisonous effect of curare is on the end-plates is the following:—The experiment described proves it is not the muscles that are paralysed. It must therefore be either the nerves, or the links between the nerve-fibres and the muscular fibres. By a process of exclusion we arrive at the conclusion that it is these links, for the following experiment shows it is not the nerves. The frog is pithed as before, and then one of its legs is tightly ligatured so as to include everything except the sciatic nerve of that leg. Curare is injected and soon spreads by the circulating blood all over the body except to the leg protected by the ligature. It can get to the sciatic nerve of that leg because that was not tied in with the rest. The sciatic nerve of the other leg is now dissected out; when the muscles supplied by it cease to contract when the nerve is stimulated, the frog may be considered to be fully under the influence of the drug. But on stimulating the sciatic nerve of the protected limb, the muscles respond normally; this shows that the nerve which has been exposed to the action of the poison has not been affected by it.

Varieties of Stimuli.

The normal stimulus that leads to muscular contraction is a nervous impulse; this is converted into a muscular impulse (visible as a contraction) at the end-plates. This nervous impulse starts at the nerve-centre, brain or spinal cord, and travels down the nerve to the muscle. In a reflex action the nervous impulse in the nerve-centre is started by a sensory impulse from the periphery; thus when one puts one's hand on something unpleasantly hot, the hand is removed; the hot object causes a nervous impulse to travel to the brain, and the brain reflects down to the muscles of the hand another impulse by the motor nerves which causes the muscles to contract in such a manner as to move the hand out of the way.

But the details of muscular contraction can be more readily studied in muscles removed from the body of such an animal as the frog, and made to contract by artificial stimuli. When we have considered these, we can return to the lessons they teach us about the normal contractions in our own bodies.

The first thing to do is to make from a pithed frog a *muscle-nerve preparation;* the muscle usually selected is the gastrocnemius, the large muscle of the calf of the leg, with the sciatic nerve attached. For some experiments the sartorius or gracilis may be used; but nearly all can be demonstrated on the gastrocnemius.

The tendon of the gastrocnemius may be tied to a lever with a flag at the end of it, and thus its contractions rendered more evident; the bone at the other end is fixed in a clamp. Stimuli may be applied either to the nerve or to the muscle. If the stimulus is applied to the nerve, it is called *indirect stimulation;* the stimulus starts a nervous impulse which travels to the muscle; the muscle is thus stimulated as it is in voluntary contraction by a nervous impulse. Stimulation of the muscle itself is called *direct stimulation.* These stimuli may be:

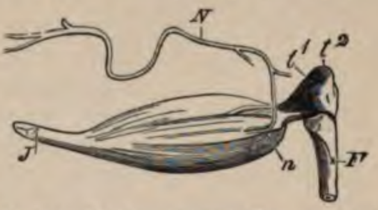


FIG. 132.—Muscle-nerve preparation. F, femur; N, nerve; T, tendo Achillis. (M'Kendrick.)

1. Mechanical; for instance a pinch or blow.
2. Chemical; for instance salt or acid sprinkled on the nerve or muscle.
3. Thermal; for instance touching the nerve or muscle with a hot wire.
4. Electrical; the constant or the induced current may be used.

In all cases the result of the stimulation is a muscular contraction. Of all methods of artificial stimulation, the electrical is the one most generally employed, because it is more under control and the strength and duration of the stimuli (shocks) can be regulated easily. We shall therefore have to study some electrical apparatus.

Chemical stimuli are peculiar, for some which affect muscle do not affect nerve, and *vice versâ;* thus glycerine stimulates nerve, but not muscle; ammonia stimulates muscle, but not motor nerves.

We may regard stimuli as liberators of energy; muscle and nerve and other irritable structures undergo disturbances in consequence of a stimulus. The disturbance is some form of movement, visible movement in the case of muscle, molecular movement in the case of nerve. A stimulus may be regarded as added motion. Sir William Gowers compares it to the blow that causes dynamite to explode, or the match applied to a train of gunpowder. A very slight blow will explode a large quantity of dynamite; a very small spark will fire a long train of gunpowder. So in muscle or nerve the effect is often out of all proportion to the strength of the stimulus; a light touch on the surface of the body may elicit very forcible nervous and muscular disturbances; and moreover, the effect of the stimulus is propagated along the nerve or muscle without loss.

CHAPTER IX

CONTRACTION OF MUSCLE

Muscle undergoes many changes when it contracts; they may be enumerated under the following five heads:—

1. Changes in form.
2. Changes in extensibility and elasticity.
3. Changes in temperature.
4. Changes in electrical condition.
5. Chemical changes.

In brief, each of these changes is as follows:—

1. *Changes in form.*—The muscle becomes shorter, and at the same time thicker. The amount of shortening varies so that the length of the muscle when contracted is from 65 to 85 per cent. of what it was originally. Up to a certain point, increase of the strength of the stimulus increases the amount of contraction. Fatigue diminishes, and up to about 33° C. the application of heat increases the amount of contraction. Beyond this temperature the muscular substance begins to be permanently contracted, and a condition called ***heat rigor***, due to coagulation of the muscle proteids, sets in a little over 40° C.

What the muscle loses in length it gains in width; there is no appreciable change of volume.

Among the changes in form must also be mentioned those changes in the individual muscular fibres which require a microscope for their investigation; these have been already considered (see p. 84).

2. *Changes in elasticity and extensibility.*—The contracted muscle is more stretched by a weight in proportion to its length than an uncontracted muscle with the same weight applied to it; the extensibility of contracted muscle is increased; its elasticity is diminished.

3. *Changes in temperature.*—When muscle is at work or contracting, more energetic chemical changes are occurring than when it is at rest; more heat is produced and its temperature rises.

4. *Changes in electrical condition.*—A muscle when it contracts undergoes a diphasic variation in its electrical condition.

5. *Chemical changes.*—These consist in an increased consumption of oxygen, and an increased output of waste materials such as carbonic acid, and sarco-lactic acid. After prolonged contraction the muscle consequently acquires an acid reaction.

These five sets of changes will form the subjects of the following five chapters.

CHAPTER X

CHANGE IN FORM IN A MUSCLE WHEN IT CONTRACTS

THOUGH it has been known since the time of Erasistratus (B.C. 304) that a muscle becomes thicker and shorter when it contracts, it was not until the invention of the *graphic method* by Ludwig and Helmholtz, about sixty years ago, that we possessed any accurate knowledge of this change. The main fact just stated may be seen by simply looking at a contracting muscle, such as the biceps of one's own arm; but more elaborate apparatus is necessary for studying the various phases in contraction and the different kinds of contraction that may occur.

These may be readily demonstrated on the ordinary muscle-nerve preparation (gastrocnemius and sciatic nerve) from a frog. By the graphic method, one means that the movement is recorded by a writing. We shall find that the same method is applied to the heart's movements, respiratory movements, blood pressure, and many other important problems in physiology. The special branch of the graphic method we have now to study is called *myography;* the instrument for writing is called a *myograph;* the writing itself is called a *myogram.* Put briefly, a myograph consists of a writing point at the end of a lever attached to the muscle, and a writing surface which travels at a uniform rate, on which the writing point inscribes its movement.

The first thing, however, that is wanted is something to stimulate the muscle and make it contract; the stimulus is usually applied to the nerve, and the form of stimulus most frequently employed is electrical.

The galvanic battery in most common use is the *Daniell cell.* It consists of a well-amalgamated zinc rod immersed in a cylinder of porous earthenware containing 10 per cent. sulphuric acid; this is contained within a copper vessel (represented as transparent for diagrammatic purposes in fig. 133) filled with saturated solution of copper sulphate. Each metal has a binding screw attached to it, to which wires can be fastened. The zinc rod is called the *positive element,* the copper the *negative element.* The distal ends of the wires attached to these are called *poles* or *electrodes*, and the pair of electrodes may be conveniently held in a special form of holder. The electrode attached to the positive element (zinc) is called the *negative pole* or *kathode;* that attached to the negative element (copper) is called the *positive pole* or *anode.* If now the two electrodes are connected together, an electrical, galvanic or *constant* current flows from the copper to the zinc outside the battery, and from the zinc to the copper through the fluids of the battery; if the electrodes are not connected the circle is broken, and no current can flow at all. If now a nerve or muscle is laid across the two electrodes the circuit is completed, and it will be noticed at the moment of completion of the circuit the muscle enters into contraction; if the muscle is lifted off the electrodes, another contraction occurs at the moment the circuit is broken. The same thing is done more conveniently by means of a key: fig. 134 represents two common forms of key. A key is a piece of apparatus by which the current can be allowed to pass or not through the nerve or muscle laid on the electrodes. When the key is open the current is broken, as in the next figure (fig. 135); when it is closed the current is allowed to pass. The opening of the key is called *break;* the closing of the key is called *make.* A contraction occurs only at make and break, not while the current is quietly traversing the nerve or muscle.

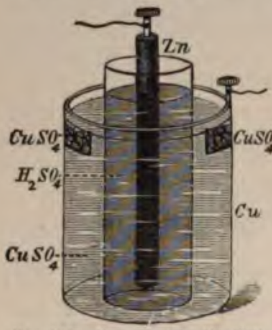
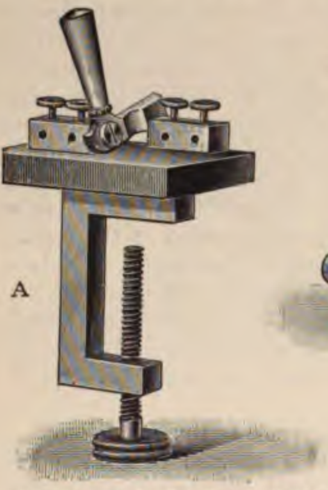
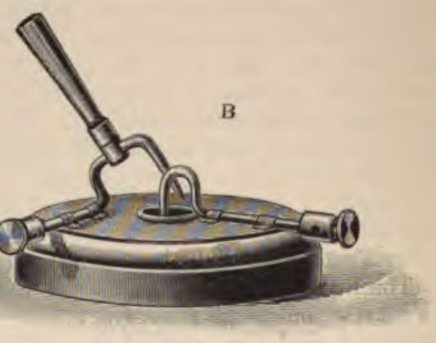


FIG. 133.—Diagram of a Daniell's Battery.





B. Mercury Key.

FIG. 134.—A. Du Bois Reymond's Key.

But it will be seen in the Du Bois Reymond key (fig. 134) that there are four binding screws. This key is used as a bridge or *short circuiting key*, and for many reasons this is the best way to use it. The next diagram (fig. 136) represents this diagrammatically. The two wires from the battery go one to each side of the key; the electrodes come off one from each side of the key. When the key is open no current can get across it, and therefore all the current has to go to the electrodes with the nerve resting on them; but when the key is closed, the current is cut off from the nerve, as then practically all of it goes by the metal bridge, or short cut, back to the battery. Theoretically a small amount of current goes through the nerve; but the resistance of animal tissues to electrical currents is enormous as compared to that of metal, and the amount of electricity that flows through a conductor is inversely proportional to the resistance; the resistance in the metal bridge is so small that for all practical purposes, all the current passes through it.

Another form of electrical stimulus is the *induced current*, produced in an induction coil.

In a battery of which the metals are connected by a wire, we have seen that the current in the wire travels from the copper to the zinc; if we have a key on the course of this wire the current can be made or broken at will. If in the neighbourhood of this wire we have a second wire forming a complete circle, nothing whatever occurs in it while the current is flowing through the first wire, but at the instant of making or breaking the current in the first or *primary wire*, a momentary electrical current occurs in the *secondary wire*, which is called an induced current; and if the secondary wire is not a complete circle, but its two ends are connected by a nerve, this induction shock traverses the nerve and stimulates it; this causes a nervous impulse to travel to the muscle, which in consequence contracts.

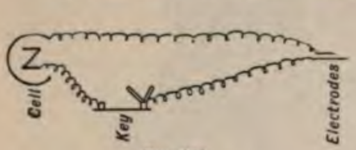


FIG. 135.

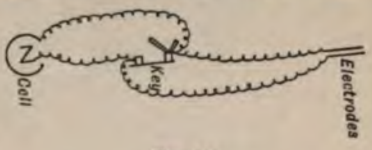


FIG. 136.

If the first and second wires are coiled many times, the effect is increased, because each turn of the primary coil acts inductively on each turn of the secondary coil.

The direction of the current induced in the secondary coil is the same as that of the current in the primary coil at the break; in the opposite direction at the make. The nearer the secondary coil is to the primary, the stronger are the currents induced in the former.

Fig. 137 represents the Du Bois Reymond coil, the one generally employed in physiological experiments. *c* is the primary coil, and *d* and *d′* its two ends, which are attached to the battery, a key being interposed for making and breaking; *g* is the secondary coil, the two terminals of which are at its far end; to these the electrodes to the nerve are attached; the distance between the two coils, and so the strength of the induction currents, can be varied at will. It is only when the primary current is made or broken, or its intensity increased or diminished, that induction shocks occur in the secondary circuit which stimulate the nerve. When one wishes to produce a rapid succession of make and break shocks the automatic interrupter or Wagner's hammer seen at the right-hand end of the diagram is included in the circuit.

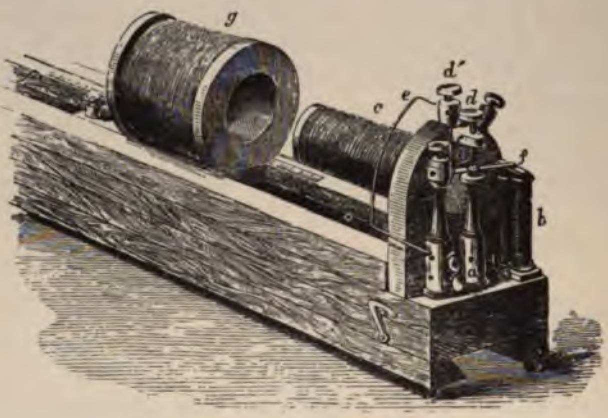


FIG. 137.—Du Bois Reymond's Induction Coil.

The next thing to be noticed is that the break effects are stronger than the make effects; this is easily felt by placing the electrodes on the tongue. This is due to what is called Faraday's extra current. This is a current produced in the primary coil by the inductive influence of contiguous turns of that wire on each other; its direction is against that of the battery current at make, and so the make shock is lessened. At the break the extra current is of such short duration (because when the circuit is broken there can be no current at all) that for all practical purposes it may be considered as non-existent.

The same difference of strength occurs alternately in the repeated shocks produced by Wagner's hammer. Helmholtz, to obviate this, introduced a modification now known after him. It consists in bridging the current by a side wire, so that the current never entirely ceases in the primary coil, but is alternately strengthened and weakened by the rise and fall of the hammer; the strengthening corresponds to the ordinary make, and is weakened by the make extra current, which occurs in the opposite direction to the battery current; the break is also incomplete, and so it is weakened by the break extra current, which being in the same direction as the battery current impedes its disappearance.

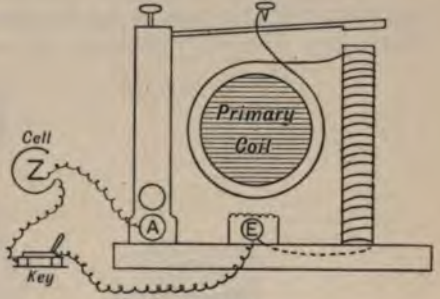


FIG. 138.

The two next diagrams show the way the interrupter acts. We are supposed to be looking at the end of the primary coil; the battery wires are attached to the binding screws A and E (fig. 138). The current now passes to the primary coil by the pillar on the left and the spring or handle of the hammer as far as the screw (C); after going round the primary coil, one turn only of which is seen, it twists round a pillar of soft iron on the right-hand side, and then to the screw E and back to the battery; the result of a current going around a bar of soft iron is to make it a magnet, so it attracts the hammer, and draws the spring away from the top screw C, and thus breaks the current; the current ceases, the soft iron is no longer a magnet, so it releases the hammer, and contact is restored by the spring; then the same thing starts over again, and so a succession of break and make shocks occurs alternately and automatically.

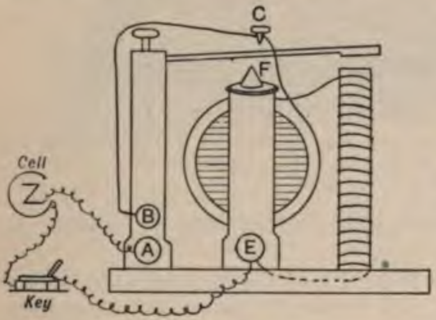


FIG. 139.

In Helmholtz's modification (fig. 139) the battery wires are connected as before. The interrupter is bridged by a wire from B to C (also shown in fig. 137, *e*). C is raised out of reach, and the lower screw F is brought within reach of the spring. Owing to the wire BC, the vibration of the hammer never entirely breaks the current.

Instead of Wagner's hammer a long vibrating reed constructed on the same principle is often used. This has the advantage that the rate of vibration can be varied at will by means of a sliding clamp which fixes the reed, so that different lengths of it can be made to vibrate. If a long piece of reed vibrates, it does so slowly, and thus successive induction shocks at long intervals can be sent into the nerve. But if one wishes to stimulate a nerve more rapidly, the length of reed allowed to vibrate can be shortened.

In Ewald's modification of the coil there is another simple method of modifying the rate of the interrupter. But an hour spent in the laboratory with an induction coil and cell will teach the student much more easily all these facts than any amount of reading and description.

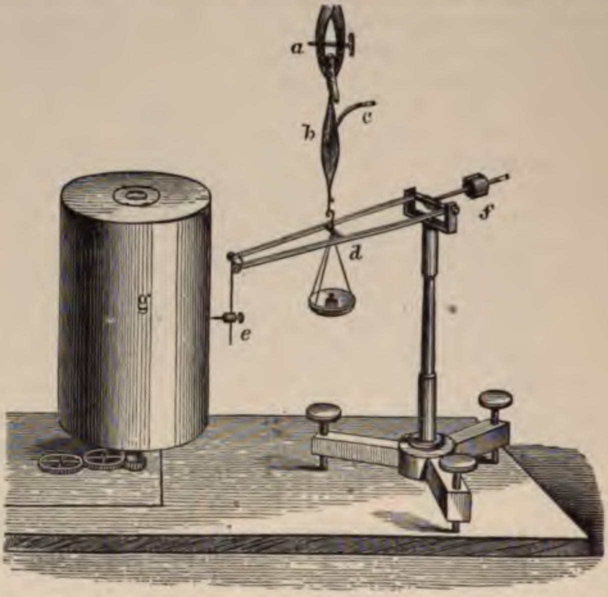


FIG. 140.—Myograph of von Helmholtz, shown in an incomplete form. *a*, forceps for holding frog's femur; *b*, gastrocnemius; *c*, sciatic nerve; *d*, scale pan; *e*, marker recording on cylinder; *f*, counterpoise. (M'Kendrick.)

We can pass now to the **myograph**. There are many different forms of this instrument. Fig. 140 shows Helmholtz's instrument.

The bony origin of the gastrocnemius is held firmly by forceps, and the tendo Achillis tied to a weighted lever; the end of the lever is provided with a writing-point such as a piece of pointed parchment; when the muscle contracts it pulls the lever up, and this movement is magnified at the end of the lever. The writing-point scratches on a piece of glazed paper covered with a layer of soot; the paper is wrapped round a cylinder. When the lever goes up the writing-point will mark an up-stroke; when it falls it will mark a down-stroke, and if the cylinder is travelling, the down-stroke will be written on a different part of the paper than the up-stroke; thus a **muscle curve** or **myogram** is obtained. The paper may then be removed, varnished, and preserved.

Fig. 141 shows a somewhat different arrangement.

The muscle is fixed horizontally on a piece of cork B, one end being fixed by a pin thrust through the knee-joint into the cork; the tendo Achillis is tied to a lever which is weighted near its fulcrum: the lever is so arranged that it rests on a screw till the muscle begins to contract; the muscle therefore does not feel the weight till it begins to contract, and gives a better contraction than if it had been previously strained by the weight. This arrangement is called *after-loading.*

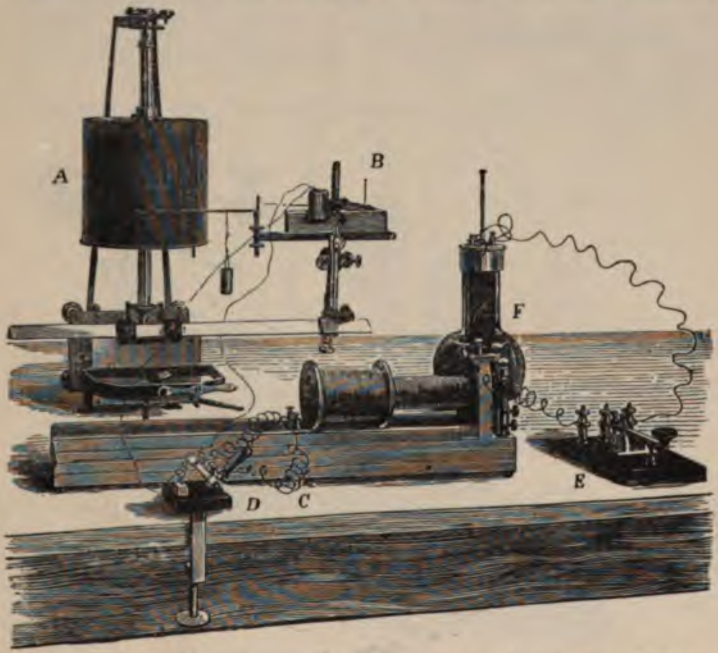


FIG. 141.—Arrangement of the apparatus necessary for recording muscle contractions with a revolving cylinder carrying smoked paper. A, revolving cylinder; B, the muscle arranged upon a cork-covered board which is capable of being raised or lowered on the upright, which also can be moved along a solid triangular bar of metal attached to the base of the recording apparatus—the tendon of the gastrocnemius is attached to the writing lever, properly weighted, by a ligature. The electrodes from the secondary coil pass to the nerve—being, for the sake of convenience, first of all brought to a short-circuiting key, D (Du Bois Reymond's); C, the induction coil; F, the battery (in this fig. a bichromate one); E, the key (Morse's) in the primary circuit.

The writing surface is again a travelling cylinder tightly covered with smoked glazed paper. The rest of the apparatus shows how cell, coil, keys, and electrodes are applied with the object of stimulating the nerve.

The key E makes and breaks the primary circuit, but the effect is only felt by the muscle-nerve preparation when the short-circuiting key D in the secondary circuit is opened.

Instead of the key E it is better to have what is called a "kick-over" key which the cylinder by means of a bar projecting from it knocks over and so breaks the primary circuit during the course of a revolution. The exact position of the writing-point at the moment of break, that is the moment of excitation, can then be marked on the blackened paper.

Besides the travelling cylinder there are other forms of writing surface. Thus fig. 142 represents the *spring myograph* of Du Bois Reymond. Here a blackened glass plate is shot along by the recoil of a spring; as it travels it kicks over a key, and the result of this, the muscular contraction, is written on the plate.

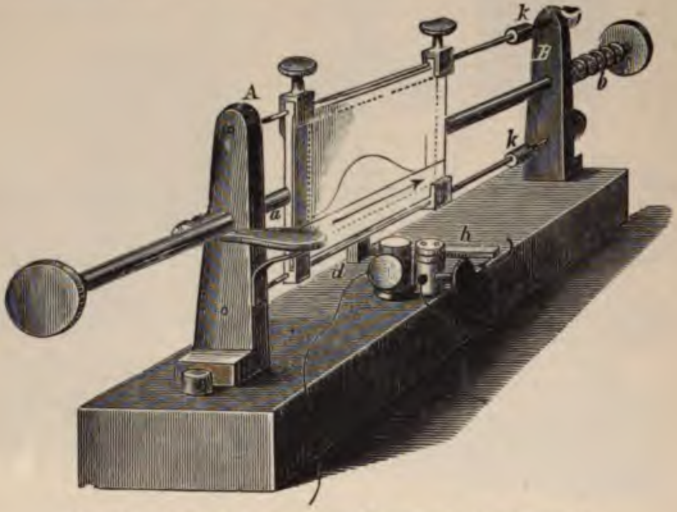


FIG. 142.—Du Bois Reymond's Spring Myograph. (M'Kendrick.)

The *pendulum myograph* (fig. 143) is another form. The pendulum carries a smoked glass plate upon which the writing-point of the muscle lever is made to mark. The break shock is sent into the muscle-nerve preparation by the pendulum in its swing opening a key in the primary circuit. This is shown in an enlarged scale in BC (fig. 143).

To keep the preparation fresh during an experiment, it should be covered with a glass shade, the air of which is kept moist by means of wet blotting-paper. A somewhat elaborate form of *moist chamber* is shown in fig. 144.

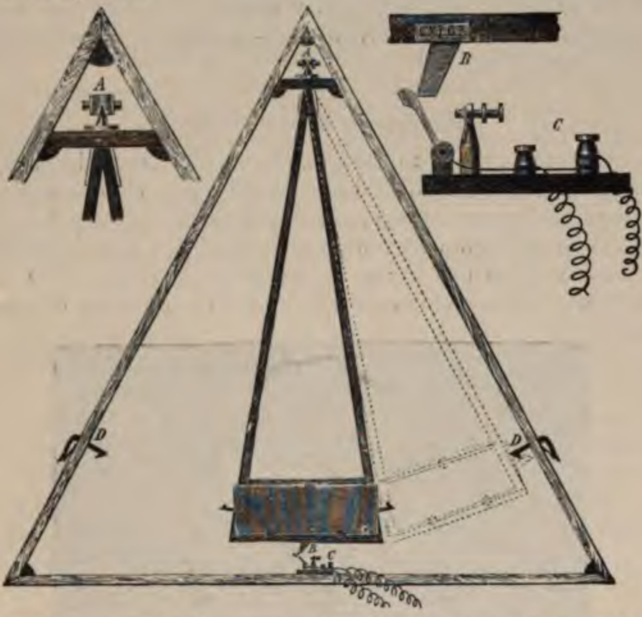


FIG. 143.—Pendulum myograph and accessory parts (Fick's pattern). *A*, pivot upon which pendulum swings; *B*, catch on lower end of myograph opening the key, *C*, in its swing; *D*, a spring-catch which retains myograph, as indicated by dotted lines, and on pressing down the handle of which the pendulum swings along the arc to *D* on the left of figure, and is caught by its spring.

The last piece of apparatus necessary is a time-marker, so that the events recorded in the myogram can be timed. The simplest

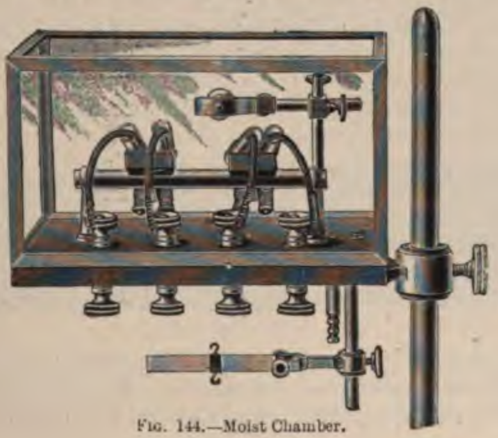


FIG. 144.—Moist Chamber.

time-marker is a tuning-fork vibrating 100 times a second. This is struck, and by means of a writing-point fixed on to one of the prongs of the fork, these vibrations may be written beneath the myogram. More elaborate forms of electrical time-markers or chronographs are frequently employed.

The Simple Muscle Curve.

We can now pass on to results, and study first the result of a single instantaneous stimulus upon a muscle. This causes a single or *simple muscular contraction*, or as it is often called a *twitch*. The graphic record of such a contraction is called the *simple muscle curve*. One of these is shown in the accompanying figure (fig. 145).

The upper line (m) is traced by the end of the lever in connection with a muscle after stimulation of the muscle by a single induction-shock: the middle-line (l) is that described by a lever, which indicates by a sudden drop the exact instant at which the induction-shock is given. The lower wavy line (t) is traced by a tuning-fork vibrating 200 times a second, and serves to measure precisely the time occupied in each part of the contraction.

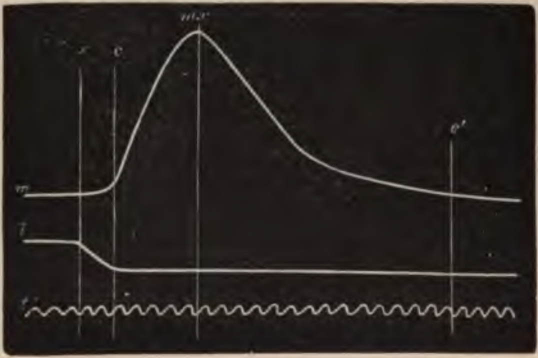


FIG. 145.—Simple muscle curve. (M. Foster.)

It will be observed that after the stimulus has been applied as indicated by the vertical line s, there is an interval before the contraction commences, as indicated by the line c. This interval, termed the **latent period**, when measured by the number of vibrations of the tuning-fork between the lines s and c, is found to be about $\frac{1}{100}$sec. During the latent period there is no *apparent* change in the muscle.

The second part is the **stage of contraction** proper. The lever is raised by the shortening of the muscle. The contraction is at first very rapid, but then progresses more slowly to its maximum, indicated by the line *mx*, drawn through its highest point. It occupies in the figure $\frac{5}{200}$sec.

The next stage is the **stage of elongation**. After reaching its highest point, the lever begins to descend, in consequence of the elongation of the muscle. At first the fall is rapid, but then becomes more gradual until the lever reaches the *abscissa* or base line, and the muscle attains its pre-contraction length, indicated in the figure by the line *c*′. The stage occupies $\frac{15}{200}$sec. Very often after the main contraction the lever rises once or twice to a slight extent, producing small curves (as in fig. 147). These contractions are simply due to the elasticity of the muscle and recording apparatus, and are most marked when the contraction is rapid and vigorous.

The whole contraction occupies about $\frac{1}{10}$ of a second. With regard to the latent period, it should be pointed out that if the muscle is stimulated indirectly, *i.e.*, through its nerve, some of the apparent lost time is occupied in the propagation of the nervous impulse along the nerve. To obtain the true latent period, this must be deducted. Then there is latency in the apparatus (friction of the lever, etc.) to be taken into account. This can be got rid of by photographing the contracting muscle, on a sensitive photographic plate travelling at an accurately-timed rate. By such means it is found that the true latent period is much shorter than was formerly supposed. It is only $\frac{1}{400}$ of a second. In red muscles it is longer.

We now come to the action of various factors in modifying the character of the simple muscle curve.

1. *Influence of strength of stimulus.*—A minimal stimulus is that which is just strong enough to give a contraction. If the strength of stimulus is increased the amount of contraction as measured by the height of the curve is increased, until a certain point is reached (maximal stimulus), beyond which increase in the stimulus produces no increase in the amount of contraction. The latent period is shorter with a strong than with a weak stimulus.

2. *Influence of load.*—Up to a certain point increase of load increases the amount of contraction, beyond which it diminishes, until at last a weight is reached which the muscle is unable to lift. The latent period is somewhat longer with a heavy load than with a light one.

3. *Influence of fatigue.*—This can be very well illustrated by letting the muscle write a curve with every revolution of the cylinder, until it ceases to contract at all. The next diagram shows the early stages of fatigue. At first the contractions improve, each being a little higher than the preceding; this is known as the *beneficial effect of contraction*, and the graphic record is called a *staircase*. Then the contractions get less and less. But what is most noticeable is that the contrac-

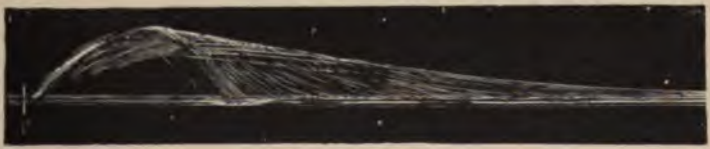


FIG. 146.—Fatigue.

tion is much more prolonged; the latent period gets longer; the period of contraction gets longer; and the period of relaxation gets very much longer; there is a condition known as *contracture*, so that the original base line is not reached by the time the next stimulus arrives. In the last stages of fatigue, contracture passes off.

4. *Effect of temperature.*—Cold at first increases the height of contraction, then diminishes it; otherwise the effect is very like that of fatigue increasing the duration of all stages of the curve.

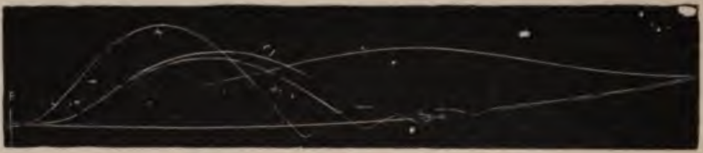


FIG. 147.—Effect of temperature on a single muscular contraction; *N*, normal; *H*, warm; *C1*, cooling; *C2*, very cold; *P*, point of stimulation. The above tracing is a considerably reduced facsimile of a tracing taken with the pendulum myograph.

Moderate warmth increases the height and diminishes the duration of all stages of the curve, latent period included. This may be readily shown by dropping some warm salt solution* on to the muscle before taking its curve. Too great heat (above 42° C.) induces *heat rigor* due to the coagulation of the muscle proteids.

5. *Effect of veratrine.*—If this is injected into the frog before the muscle-nerve preparation is made, the very remarkable result seen in the next diagram is produced on stimulation; there is an enormous prolongation of the period of relaxation; marked by a secondary rise, and sometimes by tremors. After repeated stimulation this effect passes off, but returns after a period of rest.

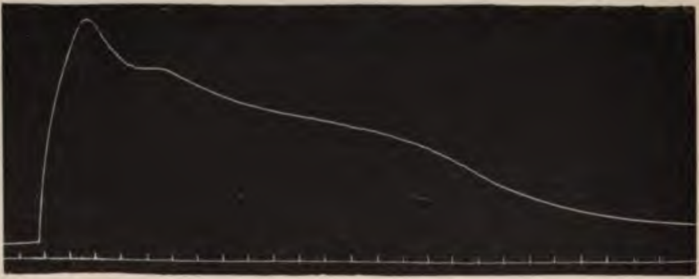


FIG. 148.—Veratrine curve, taken on a very slowly-travelling cylinder; the time tracing indicates seconds.

The Muscle-Wave.

The first part of a muscle which contracts is the part where the nerve-fibres enter; but nerve impulses are so rapidly carried to all the fibres that for practical purposes they all contract together. But in a nerveless muscle, that is one rendered physiologically nerveless by curare, if one end of the muscle is stimulated, the contraction travels as a wave of thickening to the other end of the muscle, and the rate of propagation of this wave can be recorded graphically. The next figure (fig. 149) represents one of the numerous methods that have been devised for this purpose. A muscle with long parallel fibres, like the sartorius, is taken; it is represented diagrammatically in the figure. It is stimulated at the end, where the two wires, + and −, are placed; it is grasped in two places by pincers, which are opened by the wave of thickening; the opening of the first pair of pincers (1) presses on a drum or tambour connected to a second tambour with a recording lever (1′), and this lever goes up first; the lever (2′) of the tambour connected with the second pair of pincers (2) goes up later. If the length of muscle between the pairs of pincers is measured, and by a time-tracing the delay in the raising of the second lever is ascertained, we have the arithmetical data for calculating the rate of propagation of the muscle-wave. It is about 3 metres per second in frog's muscle, but is hastened by warmth and delayed by cold and fatigue.

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* Physiological saline solution used for bathing living tissue is a 0·7 to 0·9 per cent. solution of sodium chloride in ordinary tap water.

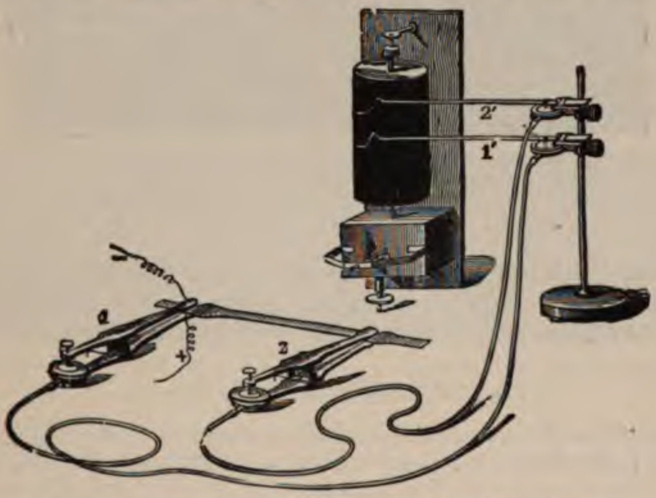

FIG. 149.—Arrangement for tracing the muscle-wave. (M'Kendrick.)

The Effect of Two successive Stimuli.

If a second stimulus follows the first stimulus, so that the muscle receives the second stimulus before it has finished contracting under the influence of the first, a second curve will be added to the first, as shown in the accompanying diagram (fig. 150). The third little curve is only due to elastic after-vibration. This is called *superposition*, or *summation of effects.*

If the two stimuli are in such close succession that the second occurs during the latent period of the first, the result will differ according as the stimuli are maximal or submaximal. If they are maximal, the second stimulus is without effect; but if submaximal the two stimuli are added together, and though producing a simple muscle-curve, produce one which is bigger than either would have produced separately. This is called *summation of stimuli.*

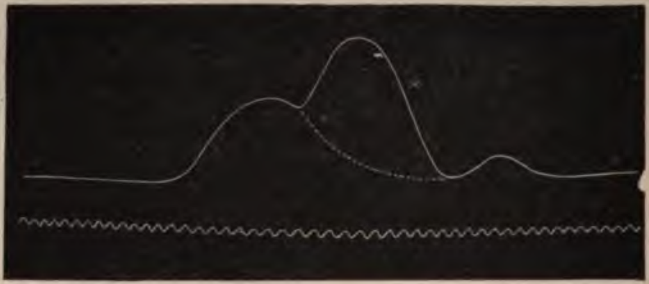

FIG. 150.—Tracing of a double muscle-curve. To be read from left to right. While the muscle was engaged in the first contraction (whose complete course, had nothing intervened, is indicated by the dotted line), a second induction-shock was thrown in, at such a time that the second contraction began just as the first was beginning to decline. The second curve is seen to start from the first, as does the first from the base line. (M. Foster.)

Effect of More than Two Stimuli.

Just as a second stimulus adds its curve to that written as the result of the first, so a third stimulus superposes its effect on the second; a fourth on the third, and so on. Each successive increment is, however, smaller than the preceding, and at last the muscle

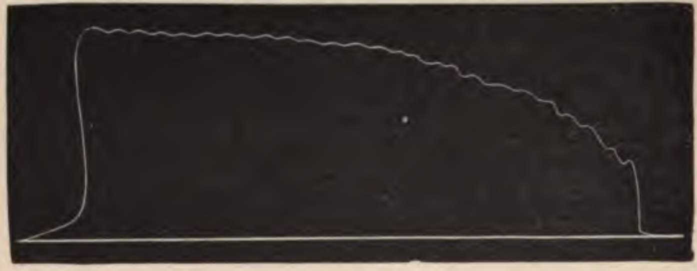

FIG. 151.—Curve of incomplete tetanus, obtained from the gastrocnemius of a frog, where the shocks were sent in from an induction coil, about sixteen times a second, by the interruption of the primary current by means of a vibrating spring, which dipped into a cup of mercury, and broke the primary current at each vibration. (Tracing to be read right to left.)

remains at a maximum contraction, till it begins to relax from fatigue.

A succession of stimuli may be sent into the nerve of a nerve-muscle preparation by means of the Wagner's hammer of a coil, or the vibrating reed previously mentioned (p. 111). This method of stimulation is called *faradisation.* Figs. 151 and 152 show the kind of tracings one obtains. The number of contractions corresponds to the number of stimulations; the condition of prolonged contraction so produced, the muscle never relaxing completely between the individual contractions of which it is made up, is called *tetanus: incomplete tetanus,* or *clonus,* when the individual contractions are discernible (fig. 151); *complete tetanus,* as in fig. 152, when the contractions are so rapid as to be completely fused to form a continuous line without waves.

The rate of faradisation necessary to cause complete tetanus varies a good deal; for frog's muscle it averages 15 to 20 per second; for the pale muscles of the rabbit, 20 per second; for the more slowly contracting red muscles of the same animal, 10 per second; and for the extremely slowly contracting muscles of the tortoise 2 per second is enough. With fatigue, the rate necessary to produce complete tetanus is diminished.

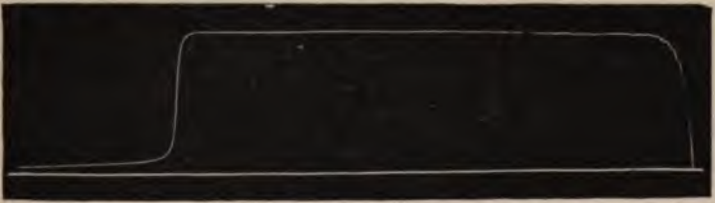

FIG. 152.—Curve of complete tetanus, from a series of very rapid shocks from a magnetic interrupter. (Tracing to be read right to left.)

Voluntary Tetanus.

We have seen that voluntary muscles under the influence of artificial stimuli may be made to contract in two ways: a single excitation causes a single contraction; a rapid series of excitations causes a series of contractions which fuse to form tetanus.

We now come to the important question, in which of these two ways does voluntary muscle ordinarily contract in the body? The answer to this is, that voluntary contraction resembles, though it is not absolutely identical with, tetanus artificially produced. It is certainly never a twitch. The nerve-cells from which the motor fibres originate do not possess the power of sending isolated impulses to the muscles; they send a series of impulses which result in a muscular tetanus,* or *voluntary tetanus*, as it may conveniently be termed.

If a stethoscope is placed over any contracting muscle of the human body, such as the biceps, a low sound is heard. The tone of this sound, which was investigated by Wollaston, and later by Helmholtz, corresponds to thirty-six vibrations per second; this was regarded as the first overtone of a note of eighteen vibrations per second, and for a long time 18 per second was believed to be the rate of voluntary tetanus.

The so-called "muscle sound" is, however, no indication of the rate of muscular vibration. Any irregular sound of low intensity will produce the same note; it is, in fact, the natural resonance-tone of the membrana tympani of the ear, and, therefore, selected by the organ of hearing when we listen to any irregular mixture of faint, low-pitched tones and noises.

A much more certain indication of the rate of voluntary tetanus is obtained by the graphic method. The myographs hitherto described are obviously inapplicable to the investigation of such a problem in man. The instrument employed is termed a *transmission myograph*. The next figure shows the recording part of the apparatus.

It is called a Marey's Tambour. It consists of a drum, on the membrane of which is a metallic disc fastened near one end of a lever, the far extremity of which carries a writing point. The interior of the drum is connected by an india-rubber tube (seen at the right-hand end of the drawing) to a second tambour called the receiving tambour, in which the writing lever is absent. Now if the receiving tambour is held in the hand, and the thumb presses on the metallic

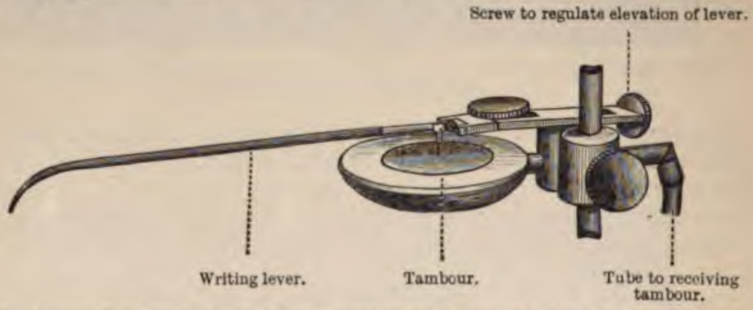
Screw to regulate elevation of lever.
Writing lever.
Tambour.
Tube to receiving tambour.

FIG. 153.—Marey's Tambour, to which the movement of the column of air in the first tambour is conducted by a tube, and from which it is communicated by the lever to a revolving cylinder, so that the tracing of the movement is obtained.

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* The use of the word tetanus in physiology must not be confounded with the disease known by the same name, in which the most marked symptom is an intense condition of muscular tetanus or cramp.

disc on the surface of its membrane, the air within it is set into vibrations of the same rate as those occurring in the thumb muscles; and these are propagated to the recording tambour and are written in a magnified form by the end of the lever on a recording travelling surface.

The tracing obtained is very like that in fig. 151; it is an incomplete tetanus, which by a time marker can be seen to be made up of 10 to 12 vibrations a second.

In some diseases these tremors are much increased, as in the clonic convulsions of epilepsy, or those produced by strychnine poisoning, but the rate is the same.

Similar tracings can be obtained in animals by strapping the receiving tambour on the surface of a muscle, and causing it to contract by stimulating the brain or spinal cord. The rate of stimulation makes no difference; however slow or fast the stimuli occur, the nerve-cells of the central nervous system give out impulses at their own normal rate.

The same is seen in a reflex action. If a tracing is taken from a frog's gastrocnemius, the muscle being left in connection with the rest of the body, its tendon only being severed and tied to a lever, and if the sciatic nerve of the other leg is cut through, and the end attached to the spinal cord is stimulated, an impulse passes up to the cells of the cord, and is then reflected down to the gastrocnemius, under observation. The impulse has thus to traverse nerve-cells; the rate of simultation then makes no difference; the reflex contraction occurs at the same rate, 10 or 12 per second.

But now a difficulty arises; if a twitch only occupies $\frac{1}{10}$ of a second, there would be time for ten complete twitches in a second; they would not fuse to form even an incomplete tetanus. There must be some means by which each individual contraction can be lengthened till it fuses with the next contraction; or, in other words, our results of electrical stimulation of excised muscles must not be applied without reserve to the contraction of the intact muscles in the living body in response to the will. Recent experiments made by Sir J. Burdon Sanderson on the electrical variation that accompanies voluntary movements, have shown that this is the case: each component of the so-called voluntary tetanus is a somewhat prolonged single contraction; a condition which closely resembles the tonic contraction of involuntary muscle.

Lever Systems.—The arrangement of the muscles, tendons, and bones presents examples of the three systems of levers which will be known to anyone who has studied mechanics; the student of anatomy will have no difficulty in finding examples of all three systems in the body. What is most striking is that the majority of cases are levers of the third kind, in which there is a loss of the mechanical power of a lever, though a gain in the rapidity and extent of the movement.

Most muscular acts involve the action of several muscles, often of many muscles. The acts of walking and running are examples of very complicated muscular actions in which it is necessary not only that many muscles should take part, but also must do so in their proper order and in due relation to the action of auxiliary and antagonistic muscles. This harmony in a complicated muscular action is called *co-ordination*.

By the device of taking instantaneous photographs at rapidly repeated intervals during a muscular act, the details of different modes of locomotion in man and other animals have been very thoroughly worked out. With this branch of research the name of Prof. Marey is intimately associated.

CHAPTER XI

EXTENSIBILITY, ELASTICITY, AND WORK OF MUSCLE

MUSCLE is both *extensible* and *elastic*. It is stretched by a weight, that is, it possesses *extensibility;* when the weight is taken off, it returns to its original length, that is, it possesses *elasticity*. The two properties do not necessarily go together; thus a piece of putty is very extensible, but it is not elastic; a piece of steel or a ball of ivory are only slightly extensible, but after the stretching force has been removed they return to their original size and shape very perfectly.

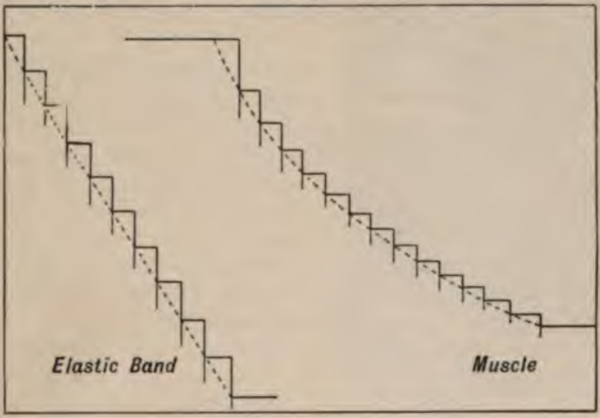

FIG. 154.—(After Waller.)

A substance is said to be *strongly elastic,* when it offers a great resistance to external forces; steel and ivory are strongly elastic.

A substance is said to be perfectly elastic, when its return to its original shape is absolute; again steel and ivory may be quoted as examples.

Muscle is very extensible, *i.e.,* it is easily stretched; it is feebly elastic, *i.e.*, it opposes no great resistance to external force; it is, however, perfectly elastic; that is, it returns to its original shape very exactly after stretching. This is true in the case of living muscle within the body, but after very great stretching even in the body, and still more so after removal from the body, when it begins to undergo degenerative changes culminating in death, its elasticity is less perfect.

The cohesion of muscular tissue is less than that of tendon. E. Weber stated that a frog's muscle one centimetre square in transverse section will support a weight of a kilogramme (over 2 lbs.) without rupture, but this diminishes as the muscle gradually dies.

The extensibility of any material may be studied and recorded by measuring the increase of length which occurs when that material is loaded with different weights. In Helmholtz's myograph (fig. 140), different weights may be placed in the scale-pan beneath the muscle, and the increase of length recorded on a stationary blackened cylinder by the downward movement of the writing point; the cylinder may then be moved on a short distance, more weight added, and the additional increase of length similarly recorded, and so on for a succession of weights.

If this experiment is done with some non-living substance, like a steel spring or a piece of india-rubber, instead of a living muscle, it is found that the amount of stretching is proportional to the weight; a weight = 2 produces an extension twice as great as that produced by a weight = 1; in this way one obtains a tracing like that seen on the left hand of figure 154, and the dotted line drawn through the lowest points of the extensions is a straight one.

With muscle, however, this is different; each successive addition of the same weight produces smaller and smaller increments of extension, and the dotted line obtained is a curve.

A continuous curve of extensibility may be obtained by placing a gradually and steadily increasing force beneath the muscle instead of a succession of weights added at intervals. The most convenient way of doing this is to use a steel spring, which is gradually and steadily extended; and the writing point connected to the muscle inscribes its excursion on a slowly moving cylinder. If, then, after the muscle has been stretched, the steel spring is gradually and steadily relaxed, the muscle retracts and again writes a curve now in the reverse direction, until it regains its original length.* But in muscles removed from the body, unless they are very slightly loaded, the return to the original length is never complete; the muscle is permanently longer to a slight extent, which varies with the amount of the previous loading.

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* A mathematical examination of these curves shows that they are not rectangular hyperbolas as they were once considered. They are very variable in form, and cannot be identified with any known mathematical curve.

If the muscle is slowly loaded and slowly unloaded, the curvature of its tracing is much more marked than if the experiment is done rapidly.

The following three tracings are reproduced from some obtained by Dr Brodie. In the method used, the records are not complicated by the curve of a lever, but the movement was simply magnified by a beam of light falling on a mirror attached to the end of the muscle, and reflected on to a travelling photographic plate. Each tracing is to be read from right to left; the first one (A) shows the result of stretching a steel spring by a steadily increasing force; the end of the spring gets lower and lower, and describes a straight line; at the apex of the tracing unloading began and went on steadily till the spring once more regained its initial length. The upstroke, like the downstroke, is a straight line. In B and C muscles were used; it will be noticed that the muscle does not regain its original length after unloading is completed, and the upward tendency of the tracing beyond this point represents after-retraction.. In B, the extension was applied rapidly, the tracing is almost a straight line; in C, the extension was brought about more slowly, and the tracing is a curve; in both cases the tracing of the period of unloading shows more curvature.

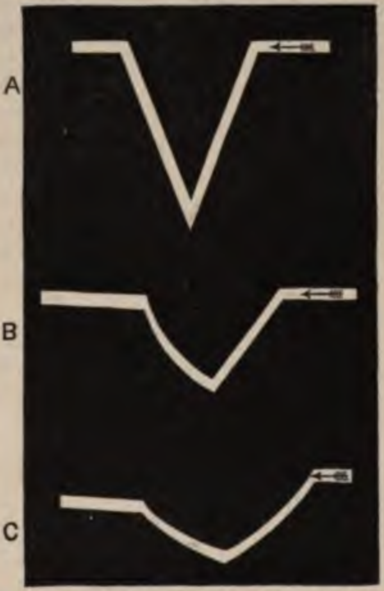


FIG. 155.—Curves of extensibility. (Brodie.)

This introduces us to what is called *after-extension* and *after-retraction*. That is to say, after a muscle is weighted there is an immediate elongation, followed by a gradual elongation which continues for some time; or if a muscle has been weighted and is then unloaded there is an immediate slackening, followed by a gradual after-retraction.

This may be shown by looking at the graphic records shown in the next diagram. It will be noticed that the extension is greatest when the muscle is in a contracted condition, and smallest when it is dead (in rigor). In fatigue the after-extension is very marked, and the return after unloading very imperfect.

We may now give the results of an actual experiment; a muscle was loaded with successive weights of 50, 100, 150, etc., grammes, and its length carefully measured in centimetres.

Load	50	100	150	200	250	300
Total extension	3·2	6	8	9·5	10	10·3
Increment of extension	—	2·8	2	1·5	0·5	0·3

Figure 156 shows that the contracted muscle is more extensible than the uncontracted muscle. This may be still further illustrated by an example given on the opposite page in the form of a diagram.

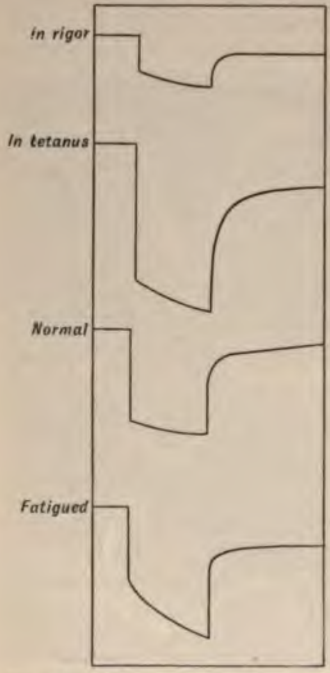


FIG. 156.—Extensibility of muscle in different states; tested by 50 grammes applied for short periods. Tracings to be read from left to right. (After Waller.)

The thick lines represent the contracted muscle, the thin ones the uncontracted. It is represented as being stretched by different weights indicated along the top line; and the lengths under the influence of these weights are separated by equal distances. Thus A C represents the length of the uncontracted muscle, A B of the contracted muscle when unloaded. A′ C′ and A′ B′ the same under the influence of a weight of 50 grammes, and so on.

The curve connecting the ends of the lengths of the contracted muscle falls faster than that obtained from the uncontracted one, until at the point P under the influence of a weight of 250 grammes, the two curves meet; that is to say, 250 grammes is the weight which the muscle is just unable to lift. Suppose a muscle has to lift the weight of 200 grammes, it begins with a length A″ C″, but when it contracts it has a length A″ B″, that is, it has contracted a distance of B″ C″, which is very small; when it has to lift a less weight it shortens more, when a greater weight it shortens less; till when it shortens least it lifts the greatest weight.

This experiment illustrates the general truth that when a muscle is contracted it is more extensible. At the point P the energy tending to shorten the muscle (its contractile power) is exactly equal to the energy tending to lengthen it against its elastic force. Thus we have the apparent paradox at this point that a muscle when contracted has exactly the same length as when uncontracted; but this is a matter of everyday experience; if one tries to lift a weight beyond one's strength, one fails to raise it, but nevertheless one's muscles have been contracting in the effort; they have not contracted in the restricted sense of becoming shorter, but that is not the only change a muscle undergoes when it contracts; the other changes, electrical, thermal, chemical, etc., have taken place, as evidenced in one's own person by the fact that the individual has got warm in his efforts, or may even feel fatigue afterwards.

But the paradox does not end here, for if diagram 157 is again looked at, it will be seen that beyond the point P the two curves cross; in other words, the muscle may even elongate due to increase of extensibility when it contracts. This is known after its discoverer as *Weber's paradox*. The increase of extensibility of muscle during contraction is protective and tends to prevent rupture in efforts to raise heavy weights.

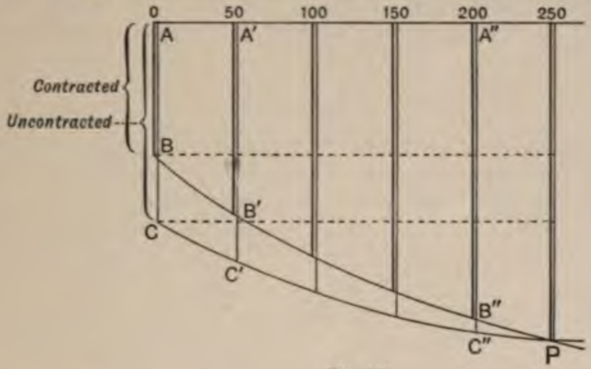


FIG. 157.

Influence of Temperature on Extensibility.—If a piece of iced india-rubber is taken and stretched by a weight, its retractility when the weight is removed is very small. If, now, when the weight is on it, it is warmed at one point as by placing the hand on it, its retractility is increased and it contracts, raising the weight. Some physiologists have considered that muscular contraction can be explained in this way; they have supposed that the heat formed in muscular contraction acts like warmth as applied to india-rubber. This view is, however, incorrect. It is much more probable that there is no causal relationship between the temperature-change and the extensibility-change which occur when muscle contracts; both are simultaneously produced by the stimulus.

Moreover, the influence of heat on muscle is by no means the same as that on india-rubber. This influence is not invariable, and at certain temperatures near the freezing-point, and under the influence of certain weights, actual elongation may occur when the temperature is raised.

Muscular Tonus.

In the living animal, muscles are more or less stretched, but never taut between their two attachments. They are in a state of *tonicity* or *tonus*, and when divided they contract and the two parts separate. Thus a muscle, even at rest, is in a favourable condition to contract without losing time or energy in taking in slack.

Muscular tonus is under the control of the nervous system (on the reflex character of this control, see later, under Tendon Reflexes); the muscles lengthen when their nerves are divided, or when they are rendered physiologically nerveless by curare. Besides the nervous system, the state of muscular nutrition dependent on a due supply of healthy blood must also be reckoned as important in maintaining muscular tonus.

Work of Muscle.

The question of muscular work is intimately associated with that of elasticity. In a technical sense, work (W) is the product of the load (l) and the height (h) to which it is raised. $W = l \times h$.

Thus in fig. 157, when the muscle is unloaded the work done is *nil:* $W = BC \times O = O$. When the load is 250, again the work done is *nil*, because then $h = O$. With the load 50, $W = B' \, C' \times 50$.

If the height is measured in feet and the load in pounds, work is expressed in terms of foot-pounds. If the height is measured in millimetres or metres, and the load in grammes, the work is expressed in gramme-millimetres or gramme-metres respectively.

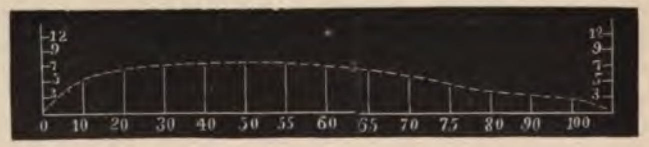


FIG. 158.—Diagram to show the mode of measuring muscle work. (M'Kendrick.)

This may be shown diagrammatically by marking on a horizontal base line or abscissa, distances proportionate to different weights, and vertical lines (ordinates) drawn through these represent the height to which they are lifted (see fig. 158).

In the diagram (fig. 158) the figures along the base line represent grammes, and the figures along the vertical line represent millimetres. The work done as indicated by the first line is $10 \times 5 = 50$

gramme-millimetres, the next 20 × 6 = 120 gramme-millimetres, and so on, while the last on the right, 100 × 3 = 300 gramme-millimetres. It is thus seen that the height of a muscle-curve is no measure of the work done by the muscle unless the weight lifted is taken into account as well.

The following figures are taken from an actual experiment done with the frog's gastrocnemius (Weber):—

Weight lifted.	Height.	Work done.
5 grammes	27·6 millimetres	138 gramme-millimetres
15 „	25·1 „	376 „
25 „	11·45 „	286 „
30 „	7·3 „	219 „

The work increases with the weight up to a certain maximum, after which a diminution occurs, more or less rapidly, according as the muscle is fatigued.

Similar experiments have been made in human beings, weights being lifted by the calf muscles, or elbow muscles, leverage being allowed for. In the higher animals the energy so obtained compared with the frog is about twice as great for the same volume of muscular tissue.

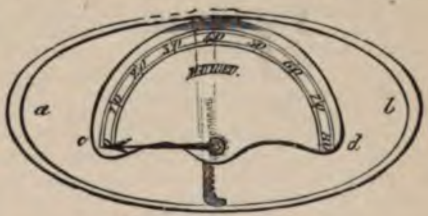


FIG. 159.—Dynamometer.

Fig. 159 represents a common form of dynamometer for clinical use, employed in testing the muscles of the arms and hands. It is squeezed by the hand, and an index represents kilogrammes of pressure.

The muscle, regarded as a machine, is sometimes compared to artificial machines like a steam-engine. A steam-engine is supplied with fuel, the latent energy of which is transformed into work and heat. The carbon of the coal unites with oxygen to form carbonic acid, and it is in this process of combustion or oxidation that heat and work are liberated. Similar, though more complicated, combustions occur in muscle. In a steam-engine a good deal of fuel is consumed, but there is great economy in the consumption of the living muscular material. Take the work done by a gramme (about 15 grains) of muscle in raising a weight of 4 grammes to the height of 4 metres (about 13 feet); in doing this work probably less than a thousandth part of the muscle has been consumed.

Next let us consider the relationship between the work and the heat produced. An ordinary locomotive wastes about 96 per cent. of its available energy as heat, only 4 per cent. being represented as work. In the best triple-expansion steam-engine the work done rises to 12·5 per cent. of the total energy.

In muscle, various experimenters give different numbers. Thus, Fick calculated that 33 per cent. of the mechanical energy is available as work; later he found this estimate too high, and stated the number as 25; Chauveau gives 12 to 15; M'Kendrick 17. Thus muscle is a little more economical that the best steam-engines; but the muscle has this great advantage over any engine, for the heat it produces is not wasted, but is used for keeping up the body temperature, the fall of which below a certain point would lead to death not only of the muscles but of the body generally.

So far we have been speaking as though the only active phase of muscular contraction is the period of shortening. It is, however, extremely probable, though not yet proved, that lengthening is also an active process. This was originally mooted by Fick, who pointed out that the fall of a muscle lever during the relaxation period is of variable speed, and is obviously not due to the passive elongation of the muscle by gravity; the way in which this part of the curve is varied by such agencies as temperature, and drugs like veratrine, also indicates that relaxation is an independent process.

Isotonic and Isometric Curves.—If, in recording the contraction of a muscle, the load is applied vertically under the muscle, its pull upon the muscle varies during the successive stages of a single contraction, owing to the inertia of the load. In order to avoid this variation in tension, it is usual to apply the weight at a point close to the fulcrum of the recording lever, so that when the lever is raised, the weight remains practically stationary, and thus the error due to its inertia is avoided. In order to apply the necessary tension to the muscle, the weight hanging on the lever must be increased in the ratio of the distances of the muscle and weight from the fulcrum. A twitch recorded under such circumstances is called *isotonic*, *i.e.*, one in which the tension remains constant throughout. If, on the other hand, the muscle is fixed at both ends, and then excited, the resulting activity expresses itself in a phase of increasing tension followed by one of decreasing tension. If the alterations of tension are recorded, we obtain what is called an *isometric* curve. This curve is obtained by making the muscle pull against a spring which is so strong that the muscle can only move it to a very slight extent. This slight movement is then highly magnified. The curve thus obtained resembles in its main features an isotonic contraction, but its maximum is reached earlier, and it returns to the zero position sooner. The flat top of the isometric curve described by the earlier observers was due to the imperfection of the instruments employed. The tracings of muscle curves given in previous illustrations (see figs. 145 to 147) were obtained by the isotonic method, but it is probable that the isometric curve is a more faithful record of the variations in the intensity of the contraction process than that yielded by the isotonic method. The momentum or swing of a light lever such as is used for obtaining isotonic curves will no doubt account for the extra upward movement it executes. The whole matter has been keenly discussed, and the foregoing view is that expressed by Kaiser. Schenk, on the other hand, maintains what appears to be an improbable idea that there are really two kinds of change in muscle, which account for the difference obtained by the two methods.

CHAPTER XII

THE ELECTRICAL PHENOMENA OF MUSCLE

WE have seen that the chemical processes occurring in muscular contraction lead to a transformation of energy into work and heat. These changes are accompanied by electrical disturbances also.

The history of animal electricity forms one of the most fascinating of chapters in physiological discovery. It dates from 1786, when Galvani made his first observations. Galvani was Professor of Anatomy and Physiology at the University of Bologna, and his wife was one day preparing some frog's legs for dinner, when she noticed that the apparently dead legs became convulsed when sparks were emitted from a frictional electrical machine which stood by. Galvani then wished to try the effect of lightning and atmospheric electricity on animal tissues. So he hung up some frogs' legs to the iron trellis-work round the roof of his house by means of copper hooks, and saw that they contracted whenever the wind blew them against the iron. He imagined this to be due to electricity secreted by the animal tissues, and this new principle was called *Galvanism*. But all his contemporaries did not agree with this idea, and most prominent among his opponents was Volta, Professor of Physics at another Italian university, Pavia. He showed that the muscular contractions were not due to animal electricity, but to artificial electricity produced by contact with different metals.

The controversy was a keen and lengthy one, and was terminated by the death of Galvani in 1798. Before he died, however, he gave to the world the experiment known as "contraction without metals," which we shall study presently, and which conclusively proved the existence of animal electricity. Volta, however, never believed in it. In his hand electricity took a physical turn, and the year after Galvani's death he invented the Voltaic pile, the progenitor of our modern batteries. Volta was right in maintaining that galvanism can be produced independently of animals, but wrong in denying that electrical currents could be obtained from animal tissues. Galvani was right in maintaining the existence of animal electricity, but wrong in supposing that the contact of dissimilar metals with tissues proved his point.

This conclusion has been arrived at by certain new methods of investigation. In 1820 Oersted discovered electro-magnetism: that is, when a galvanic current passes along a wire near a magnetic needle, the needle is deflected one way or the other, according to the direction of the current. This led to the invention of the astatic needle and the galvanometer, an instrument by which very weak electrical currents can be detected. For a long time the subject of animal electricity, however, fell largely into disrepute, because of the quackery that grew up around it. It is not entirely free from this evil nowadays; but the scientific investigation of the subject has led to a considerable increase of knowledge, and among the names of modern physiologists associated with it must be particularly mentioned those of Du Bois Reymond and Hermann.

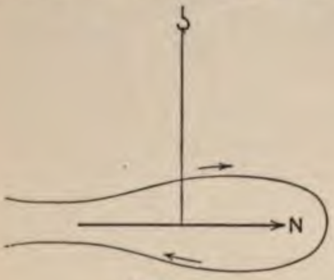


Fig. 160.

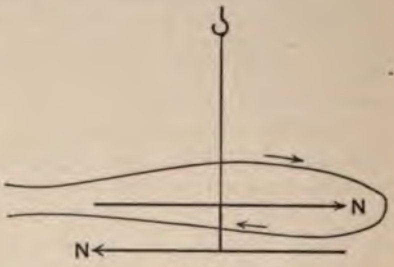
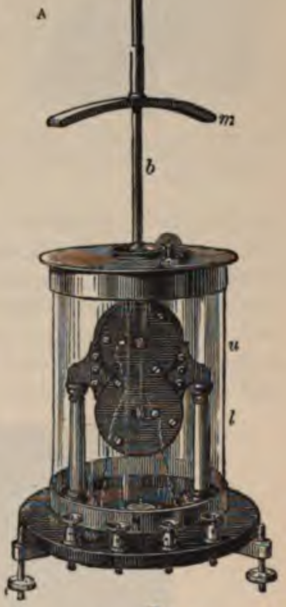


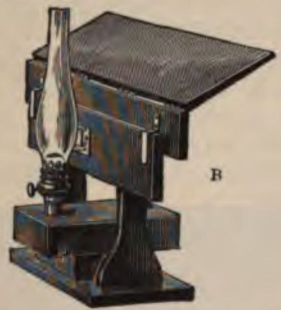
Fig. 161.

Before we can study these it is, however, necessary that we should understand the instruments employed.

The Galvanometer.—The essential part of a galvanometer is a magnetic needle suspended by a delicate thread; a wire coils round it; and if a current flows through the wire, the needle is deflected. Suppose a man to be swimming with the current with his face to the needle, the north-seeking pole is turned to the left hand. But such a simple instrument as that shown in fig. 160 would not detect the feeble currents obtained from animal tissues. It is necessary to increase the delicacy of the apparatus, and this is done in several ways. In the first place, the needle must be rendered *astatic*, that is, independent of the earth's magnetism. The simplest way of doing this is to fix two needles together (as shown in fig. 161), the north pole of one pointing the same way as the south pole of the other. The current is led over one needle and then over the other; the effect is to produce a deflection in each in the same direction, and so the sensitiveness of the instrument is doubled. If now the wire is coiled not only once, but twice or more in the same position, each coil has its effect on the needles; the multiplication of the effect of a weak current in this way is accomplished in actual galvanometers by many hundreds of turns of fine wire.

Fig. 162 illustrates the best galvanometer: that of Sir William Thomson (now Lord Kelvin). It is called a reflecting galvanometer, because the observer does not actually watch the moving needle, but a spot of light reflected on to a scale from a little mirror, which is attached to and moves with the needle. A very small movement of the needle is rendered evident, because the movement of the spot of light being, as it were, at the end of a long lever—namely, the beam of light, magnifies it.





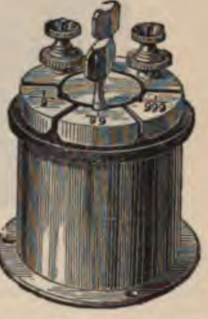


FIG. 162.—Reflecting galvanometer. (Thomson.) A. The galvanometer consists of two systems of small astatic needles suspended by a fine hair from a support, so that each set of needles is within a coil of fine insulated copper wire, that forming the lower coil being wound in an opposite direction to the upper. Attached to the upper set of needles is a small mirror about ¼ inch in diameter; the light from the lamp at B is thrown upon this little mirror, and is reflected upon the scale on the other side of B, not shown in figure. The coils *u l* are arranged upon brass uprights, and their ends are carried to the binding screws. The whole apparatus is placed upon a vulcanite plate capable of being levelled by the screw supports, and is covered by a brass-bound glass shade, the cover of which is also of brass, and supports a brass rod *b*, on which moves a weak curved magnet *m*. C is the shunt by means of which the amount of the current sent into the galvanometer may be regulated. When in use the scale is placed about three feet from the galvanometer, which is arranged east and west, the lamp is lighted, the mirror is made to swing, and the light from the lamp is adjusted to fall upon it, and it is then regulated until the reflected spot of light from it falls upon the zero of the scale. The wires from the non-polarisable electrodes touching the muscle are attached to the outer binding screws of the galvanometer, a key intervening for short circuiting, or if a portion only of the current is to pass into the galvanometer, the shunt should intervene as well with the appropriate plug in. When a current passes into the galvanometer the needles and, with them, the mirror, are turned to the right or left according to the direction of the current. The amount of the deflection of the needle is marked on the scale by the spot of light travelling along it.

Non-polarisable Electrodes.—If a galvanometer is connected with a muscle by wires which touch the muscle, electrical currents are obtained in the circuit which are set up by the contact of metal with muscle. The currents so obtained form no evidence of electromotive force in the muscle itself. It is therefore necessary that the wires from the galvanometer should have interposed between them and the muscle some form of electrodes which are non-polarisable. Fig. 163 shows one of the earliest non-polarisable electrodes of Du Bois Reymond. It consists of a zinc trough on a vulcanite base. The inner surface of the trough is amalgamated and nearly filled with a saturated solution of zinc sulphate. In the trough is placed a cushion of blotting-paper, which projects over the edge of the trough; on it there is a pad of china clay or kaolin, moistened with physiological salt solution (0·8 per cent. NaCl); on this pad one end of the muscle rests. The binding screw (k) connects the instrument to the galvanometer; the other end, or some other part of the same muscle, is connected by another non-polarisable electrode in the same way to the other side of the galvanometer. If there is any electrical difference of potential (that is, difference in amount of positive or negative electricity) between the two parts of the muscle thus led off, there will be a swing of the galvanometer needle; the galvanometer detects the existence and direction of any current that occurs.

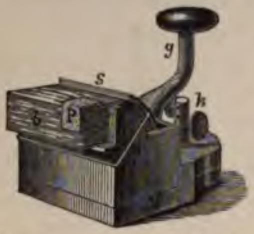


FIG. 163.—Non-polarisable electrode of Du Bois Reymond. (M'Kendrick.)

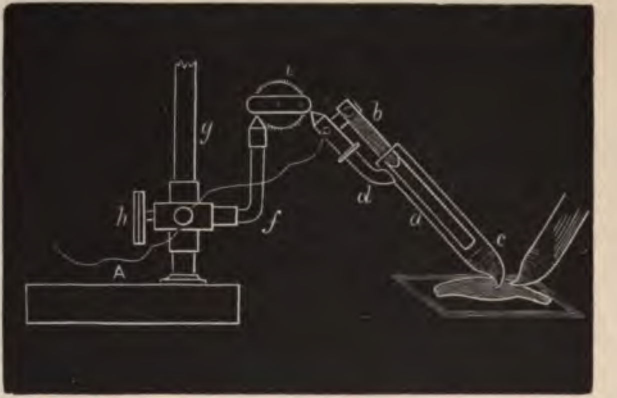


FIG. 164.—Diagram of Du Bois Reymond's non-polarisable electrodes. a, glass tube filled with a saturated solution of zinc sulphate, in the end, c, of which is china clay drawn out to a point; the clay is moistened with 0·8 NaCl solution; in the solution a well amalgamated zinc rod is immersed and connected, by means of the wire A, with the galvanometer. The remainder of the apparatus is simply for convenience of application. The muscle and the end of the second electrode are to the right of the figure.

Fig. 164 shows a more convenient form of non-polarisable electrodes.

In order to measure the strength (electromotive force) of such currents, the mere amount of swing of the needle is only a very rough indication, and in accurate work the arrangement shown in fig. 165 must be used. The electromotive force is usually measured in terms of a standard Daniell cell. The two surfaces of the muscle (M) are led off to a galvanometer (B); the needle swings, and then a fraction of a Daniell cell is introduced in the reverse direction so as to neutralise the muscle current, and bring back the needle to rest. From the Daniell cell K, wires pass to the ends *a*, *b* of a long platinum wire of high resistance, called the compensator; *c* is a slider on this wire; *a* and *c* are connected to the galvanometer, the commutator C enabling the observer to ensure that the current from the Daniell passes in the opposite direction to that produced by the muscle. If the slider *c* is placed at the end *b* of the compensator, the whole strength of the Daniell will be sent through the galvanometer and will more than

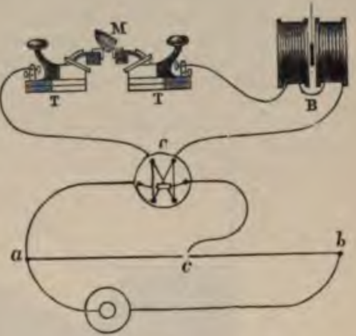


Fig. 165.—Arrangement for measuring the electromotive force of muscle. (M'Kendrick.)

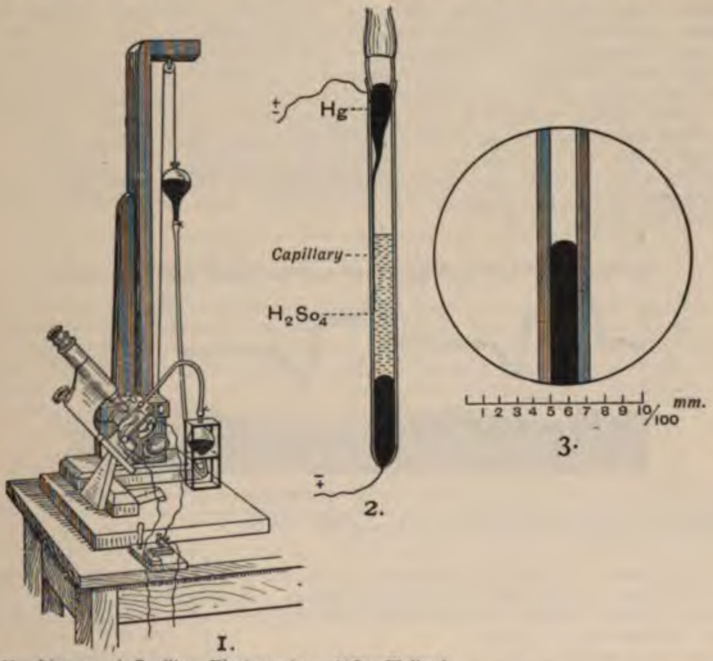


Fig. 166.—Lippmann's Capillary Electrometer. (After Waller.)
1. Pressure apparatus and microscope on stand of which the capillary tube is fixed.
2. Capillary tube, fixed in outer tube containing 10 per cent. sulphuric acid; the platinum wires are also shown.
3. Capillary and column of mercury as seen in the field of the microscope.

neutralise the muscle current; if *c* is half way between *a* and *b*, half the Daniell's strength will be sent in; but this is also too much; *ac* will be found to be only quite a small fraction of *ab*; and this fraction will correspond to a proportional fraction of the electromotive force of the Daniell cell.

Lippmann's Capillary Electrometer.—This instrument is often used instead of the galvanometer. It consists of a glass tube drawn out at one end to a fine capillary and filled with mercury. It is connected to an apparatus by which the pressure on this mercury can be lowered or increased. The open capillary tube is enclosed within another tube filled with 10 per cent. sulphuric acid. Two platinum wires fused through the glass, pass respectively into the mercury and the acid, and the other ends of these wires are connected by electrodes to two portions of the surface of a muscle. The capillary tube is observed by a microscope (see fig. 166). The surface of the mercury is in a state of tension which is easily increased or diminished by variations of electrical potential, and the mercury moves in the direction of the negative pole.

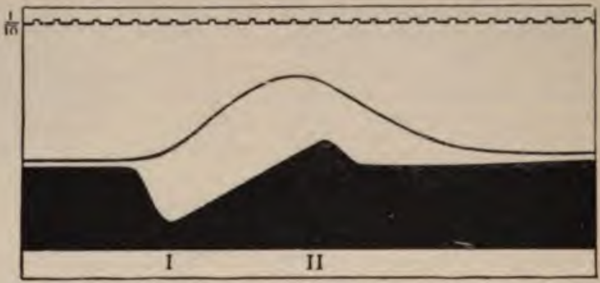


FIG. 167.—Frog's heart. Diphasic variation. Simultaneous photograph of a single beat (upper black line), and the accompanying electrical change indicated by the level of the black area, which shows the varying level of mercury in a capillary electrometer. (Waller.)

If the shadow of the mercurial column is thrown upon a travelling sensitive photographic plate, photographs are obtained which show the electrical variations in a living tissue in a graphic manner. The instrument is exceedingly sensitive, and its indications are practically instantaneous. Figs. 167 and 168 indicate the kind of result one obtains with the heart, which will be more fully discussed when we are considering that organ.

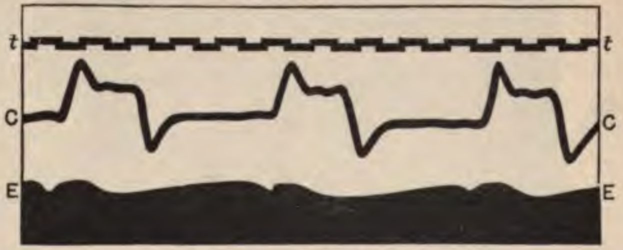


FIG. 168.—Human heart. Diphasic variation, EE, and simultaneous cardiogram, CC. Time *tt* is marked in $\frac{1}{10}$th second. The lead-offs to the capillary electrometer were from the mouth to the sulphuric acid, and from the left foot to the mercury. (Waller.)

The Rheotome.—This is an instrument by means of which the time of the occurrence of electrical disturbances in relation to the contraction of a muscle can be determined. This is in principle effected by a revolving bar carrying two contacts, one in the primary or exciting circuit (1, 1, 1, 1), one in the galvanometer circuit

(2, 2, 2, 2). The bar revolves, and by making or breaking the primary circuit sends an induction shock into the nerve at the same instant.

The muscle is connected by non-polarisable electrodes to the galvanometer; this circuit includes the brass blocks 2, 2, on the disc over which the bar revolves, and a compensator not shown in the figure to neutralise any current set up by the muscle in a state of rest. If an electrical change occurs in the muscle, it is only noticed by the galvanometer if at the same time the bar on its revolution connects the two brass blocks on the disc, and so completes the circuit. The apparatus can be set so that the bar makes the primary contact (1, 1) simultaneously with the galvanometer contacts, or that the galvanometer contact is made, 1, 2, 3, etc., hundredths of a second later than the primary contact. If the two are closed simultaneously the electrical condition of the muscle is tapped off at the moment of excitation; if the galvanometer contact is closed $\frac{1}{100}$, $\frac{2}{100}$, $\frac{3}{100}$, etc. second after excitation, the electrical condition of the muscle at that particular instant is ascertained. By a number of experiments with different intervals between the making of the two contacts, one ascertains how long after the excitation the change in the electrical condition of the muscle takes place.

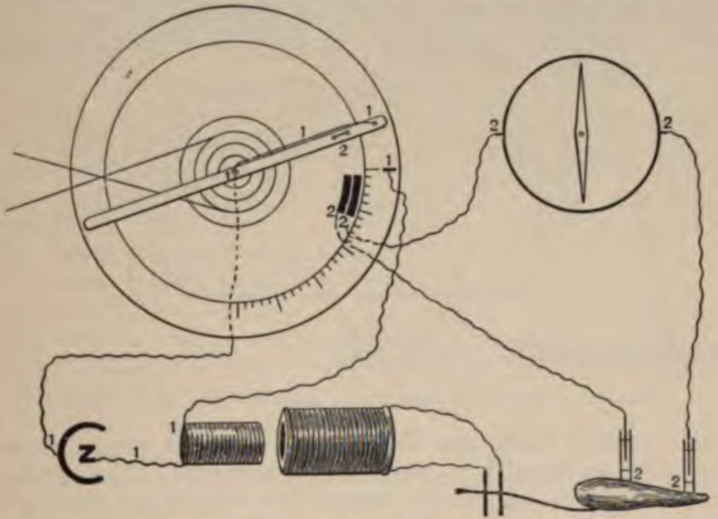


FIG. 169.—Scheme of a Rheotome. (Waller.)

We can now pass on to a consideration of results.

In muscles that are removed from the body, it is found that on leading off two parts of their surface to a galvanometer, the galvanometer needle generally swings. The most marked result is obtained with a piece of muscle in which the fibres run parallel to one another, and the longitudinal surface is connected with one of the cut ends by a wire (2 in fig. 170).

On the course of the wire a galvanometer indicates that a current flows from the centre to the cut end outside the muscle, and from the cut end to the centre inside the muscle. If, now, the muscle is thrown into tetanic contraction, the needle returns more or less completely to the position of rest.

Du Bois Reymond, who first described these facts, called the first current the *current of rest*, and the second current, the *current of action*; the change in direction is indicated by the expression *negative variation*; this means that the current of action is in the opposite direction to the current of rest, and therefore lessens or neutralises it. The word negative is therefore used in its arithmetical, not its electrical sense. Du Bois Reymond explained this by supposing that a muscular fibre is built up of molecules, each of which is galvanometrically positive in the centre and galvanometrically negative at both ends. So when a muscle is cut across, a number of the galvanometrically negative ends of these molecules is exposed. On contraction the difference between the centre and ends of each molecule is lessened, and the resultant effect on the whole muscle (made up of such molecules) is similar.

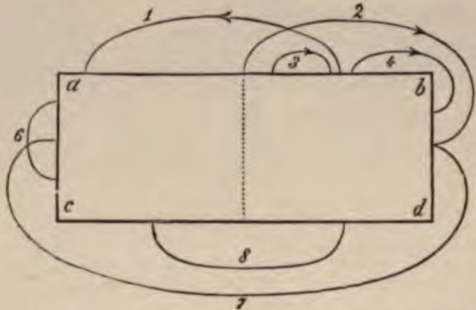


FIG. 170.—Diagram of the currents in a muscle prism. (Du Bois Reymond.)

In the foregoing sentence I have employed the rather cumbrous adjectives, *galvanometrically positive* and *galvanometrically negative*, instead of the terms positive and negative which are usually employed by physiologists.

If we take a Daniell cell and connect it to a galvanometer, the zinc, as we have seen, is the electro-positive element, and the copper the electro-negative element, but the ends of the wires which connect these metals to the galvanometer have the reverse names; the kathode or negative pole is connected to the zinc or positive metal; the anode or positive pole is connected to the copper or negative metal. The current enters the galvanometer by the anode, and leaves it on its way back to the zinc by the kathode. Therefore, although the copper is electro-negative, it may be spoken of as galvanometrically positive, and the zinc though electro-positive, as galvanometrically negative.

If we apply this to a muscle, we have seen that the current flows (in the wire that connects the uninjured longitudinal surface to the cut end) from the longitudinal surface to the cut end; the longitudinal surface thus corresponds to the copper of the Daniell cell, and is therefore electro-negative, though galvanometrically positive; similarly the cut end corresponds to the zinc, and is electro-positive though galvanometrically negative.

The omission of the qualifying prefix to positive and negative has led to a good deal of confusion in physiological writings. A physicist uses the terms positive and negative as meaning electro-positive and electro-negative respectively, and as Dr Waller has pointed out, it is time that physiologists adopted the same nomenclature. In what now follows, I propose to adopt Dr Waller's suggestion.

There is no doubt about the facts as described by Du Bois Reymond. We now adopt, however, an entirely different view of their meaning: in causing this revolution of ideas the principal part has been played by Hermann. Hermann showed that the so-called current of rest does not exist; it is really a current produced by injury, and is now generally called a *demarcation current:* the more the ends of the muscle are injured the more positive they become; and when they are connected to the uninjured centre, a current naturally is set up as described by Du Bois Reymond. If a muscle is at rest and absolutely uninjured it is iso-electric; that is, it gives no current at all when two parts of it are connected together by a wire.

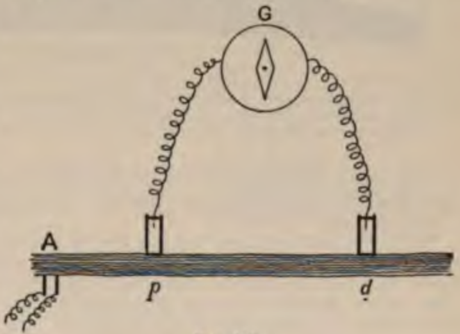


FIG. 171.

Since Du Bois Reymond's researches, the electrical changes which occur during a single twitch have been studied also, and before we can understand the "negative variation" of tetanus, it is obviously necessary to consider the electrical variation which takes place during a twitch, for tetanus is made up of a fused series of twitches.

The electrical change during a twitch is called a *diphasic variation.* The contracting part of a muscle becomes first more positive than it was before; it then rapidly returns to its previously negative condition. The increase of positivity indicates a disturbance of the stability of the tissue; the disappearance of this increased positivity is the result of a return of the muscular tissue to a state of rest. If the muscle is stimulated at one end, a wave of contraction travels along it to the other end. This muscle-wave (see p. 118) may be most readily studied in a curarised muscle, that is, in a muscle which is physiologically nerveless. The electrical variation travels at the same rate as the visible contraction, but precedes it.

Suppose two points (*p*) and (*d*) of the muscle are connected by non-polarisable electrodes to a galvanometer, and that the muscle-wave is started by a single stimulus applied at A; as soon as the wave reaches (*p*) this point becomes positive to (*d*), and therefore a current flows from (*d*) to (*p*) through the galvanometer (G). A moment later the two points are equi-potential and no current flows;

a minute fraction of a second* later this balance is upset, and now when the wave reaches the point (*d*), that point is positive to (*p*), and the galvanometer needle moves in the opposite direction.

The electrical variations may also be investigated by the capillary electrometer; the mercury moves first in one direction, and then in the other. The deep black curve in the next figure (fig. 172) shows the record obtaining by photographing the movement of the column of mercury on a rapidly travelling photographic plate.

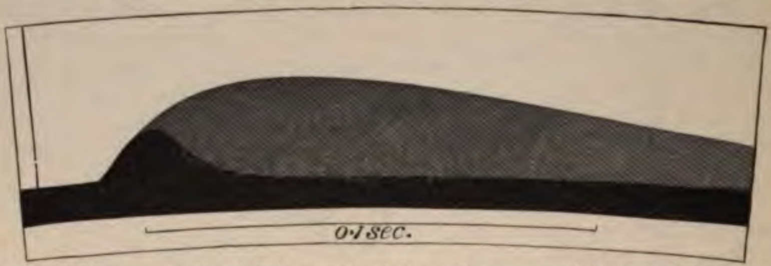


FIG. 172.—Diphasic curve (black) of the normal sartorius. The grey curve is the monophasic curve of the same muscle when one electrometer contact was placed on the injured end. The two photographic curves are placed one over the other so that the beginnings coincide. (Burdon Sanderson.)

The capillary electrometer has the advantage of giving us the means of measuring the time of onset and duration of the electrical disturbance, and experiments made with this instrument confirm the earlier experiments made with the rheotome. They show that the change only lasts a few thousandths of a second, and is over long before the other changes in form, etc., are completed. Sir J. Burdon Sanderson gives the following numbers from experiments with the frog's gastrocnemius. When the muscle was excited through its nerve the electrical response began $\frac{4}{1000}$ and the change of form $\frac{8}{1000}$ second after the stimulation; the second phase of the electrical response began $\frac{11}{1000}$ second after excitation. When the muscle was directly excited, the latent period was much shorter, the change in form beginning $\frac{4}{1000}$ and the electrical change in less than $\frac{1}{1000}$ second after excitation.

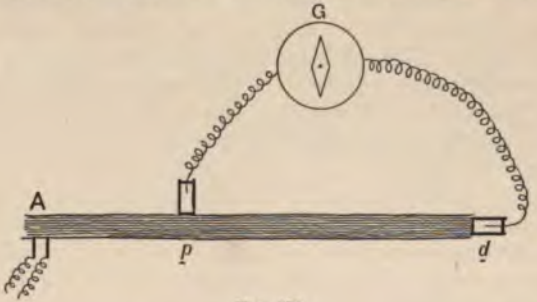


FIG. 173.

If, however, instead of examining the electrical change in the muscle in the manner depicted in fig. 171, one electrode is placed on the uninjured surface and the other on the cut end (see fig. 173), the electrical response is a different one.

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* The time will vary with the distance between (*p*) and (*d*).

Under these circumstances, the electrical change is a *monophasic variation*, for when the muscle-wave reaches (*d*), this part of the muscle, owing to its injured state, does not respond to the excitatory condition, and the electrical response is also extinguished.

The grey curve in fig. 172 is the graphic record of the change as revealed by the capillary electrometer. It will be seen that the ascending limb of the curve is identical in the two cases, but that the second phase is absent. From the point at which the diphasic curve approaches its culmination the injury curve diverges from it, continuing to ascend; the line soon after becomes horizontal, and then begins slowly to decline. This long tail denotes only the gradual disappearance of polarisation of the mercury meniscus.

The meaning of such photographic records becomes clear by testing the electrometer with known differences of potential, and from such data it is possible to construct what may be called an interpretation diagram (fig. 174). The horizontal line is that of equipotentiality of the two surfaces of contact (*p*) and (*d*). The curve P′ expresses the relative positivity of the surface (*p*); the curve D′, the corresponding relative positivity of the surface (*d*). S′ is a curve of which the ordinates are the algebraic sums of the corresponding ordinates of P′ and D′. S is the photographic curve which expresses S′; P is the photographic curve which expresses P′ (monophasic variation). The numbers under the horizontal line indicate hundredths of a second; the distance *t t′* expresses the time taken by the wave in its progress from (*p*) to (*d*).

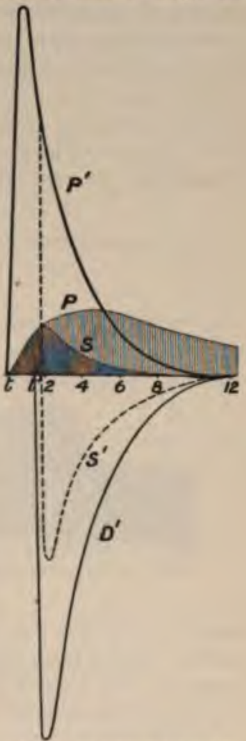

FIG. 174.—Interpretation diagram. (Burdon Sanderson.)

From these considerations we can now pass to study what occurs when the muscle enters into tetanus. The simplest case is that which was first observed by Du Bois Reymond. He placed his non-polarisable electrodes in the positions indicated in fig. 173, one (*p*) on the comparatively uninjured surface, the other (*d*) on the devitalised cut end. He sent in the tetanising series of shocks at A. The electrical response is under these circumstances a summation of the individual electrical responses evoked by instantaneous stimuli; and the monophasic character of the single response explains easily what occurs during tetanus; the centre of the muscle becomes more positive than it was before, and so the electrical difference of potential between the centre and the injured end is lessened. But with regard to uninjured muscle the problem is not so easy. It is at first sight difficult to see why the summed effects of a series of diphasic variations should take the direction of the first phase, as was found to be the case by Du Bois Reymond in experiments with the frog's gastrocnemius. One would have anticipated that "negative" variation in the arithmetical sense would be absent altogether, and this is the case in absolutely normal muscles; Hermann has shown that it is so during tetanus of the human forearm. But a muscle removed from an animal's body cannot be considered absolutely normal, and if the two contacts be placed on the comparatively uninjured longitudinal surface, as in fig. 171, a negative variation is observed, each excitatory phase becoming weaker as it progresses, and the second phase of each diphasic effect is weaker than the first. The following figure illustrates the record obtained by the capillary electrometer from an injured sartorius excited 14 times a second; each oscillation represents a single monophasic variation. The individual oscillations can, however, be seen when the excitations follow one another more rapidly, even up to 80 or 100 per second.

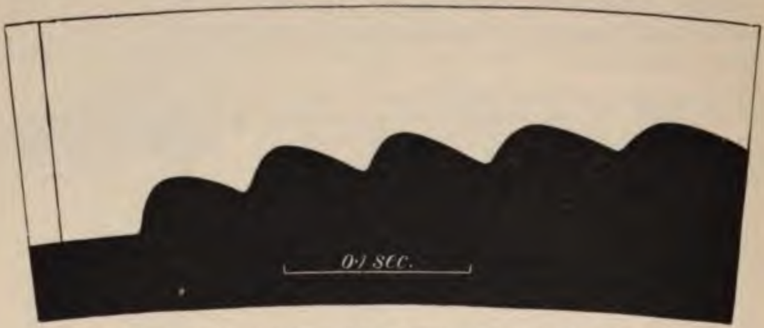

FIG. 175.—Electrometer record of injured sartorius during tetanus. (Burdon Sanderson.)

Muscle is not the only tissue which exhibits electrical phenomena. A nerve which is uninjured is iso-electric; injury causes a demarcation current; activity is accompanied with a similar diphasic wave travelling along the nerve simultaneously with the nervous impulse. The activity of secreting glands, vegetable tissues, retina, etc., is accompanied with somewhat similar electrical changes, which we shall study in detail later.

But the most prominent exhibition of animal electricity is seen in the electric organs of electric fishes. In some of these fishes the electric organ is modified muscle, in which a series, as it were, of hypertrophied end-plates correspond to the plates in a voltaic pile. In other fishes the electric organ is composed of modified skin glands.

But in each case the electric discharge is the principal phenomenon that accompanies activity.

The Rheoscopic Frog.

The electrical changes in muscle can be detected not only by the galvanometer and electrometer, but also by what is known as the *physiological rheoscope;* this consists of an ordinary muscle-nerve preparation from a fresh and vigorous frog. The nerve is stimulated by the electrical changes occurring in muscles, and the nervous impulse so generated causes a contraction of the muscles of the rheoscopic preparation. The following are the principal experiments that can be shown in this way:—

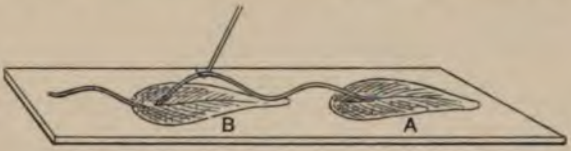

FIG. 176.—Galvani's experiment without metals.

1. *Contraction without metals.* If the nerve of a nerve-muscle preparation A is dropped upon another muscle B (fig. 176) or upon its own muscle, it will be stimulated by the injury current of the muscle on which it is dropped, and this leads to a contraction of the muscle (A) which it supplies. The experiment succeeds best if the nerve is dropped across a longitudinal surface and a freshly made transverse section.

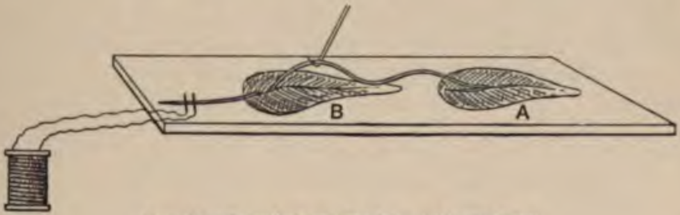

FIG. 177.—Secondary contraction. (After Waller.)

2. *Secondary contraction.* This is caused by the current of action. If, while the nerve of A is resting on the muscle B (fig. 177), the latter is made to contract by the stimulation of its nerve, the nerve of A is stimulated by the electrical variation which accompanies the contraction of the muscle B, and so a contraction of muscle A is produced. This is called *secondary contraction.* It may be either a secondary twitch or secondary tetanus.

according as to whether the muscle B is made to contract singly or tetanically.

3. *Secondary contraction from the heart.* If an excised but still beating frog's heart is used instead of muscle B, and the nerve of A laid across it, each heart's beat, accompanied as it is by an electrical variation, will stimulate the nerve and cause a twitch in the rheoscopic muscle A.

CHAPTER XIII

THERMAL AND CHEMICAL CHANGES IN MUSCLE

In muscular contraction there is a transformation of the potential energy of chemical affinity into other forms of energy, especially molar motion and heat. Heat is a form of motion in which there is movement of molecules; in molar motion there is movement of masses. The fact that when a blacksmith hammers a piece of iron it becomes hot is a familiar illustration of the transformation of one mode of movement into the other. Heat is measured in heat-units or calories. One calorie is the energy required to raise the temperature of 1 gramme of water from 0° to 1° C.; and this in terms of work is equal to 425·5 gramme-metres, that is, the energy required to raise the weight of 425·5 grammes to the height of 1 metre.

A muscle when uncontracted is nevertheless not at absolute rest. We have already seen that it possesses tonus or tone; it also possesses what we may call chemical tone; that is, chemical changes are occurring in it, and consequently heat is being produced. But when it contracts, the liberation of energy is increased; work is done, and more heat is produced; the heat produced represents more of the energy than the work done. The more resistance that is offered to a muscular contraction, the more is the work done relatively increased and the heat diminished. The amount of heat produced is increased by increasing the tension of the muscle. It diminishes as fatigue comes on. On increasing the strength of the stimulus the amount of heat increases faster, proportionately, than the work performed.

If work is done by a few large contractions, more heat is produced than if the same work is done by a larger number of smaller contractions; that is, more chemical decomposition occurs, and fatigue ensues more rapidly in the first case. This fact is within the personal experience of everyone. If one ascends a tower, the work done is the raising of the weight of one's body to the top of the tower. If the staircase in the tower has a gentle slope, each stair being low, far less fatigue is experienced than if one ascended to the same height by a smaller number of steeper steps.

On a cold day one keeps oneself warm by muscular exercise; this common fact is confirmed by more accurate experiments on isolated muscles, the heat produced being sufficient to raise temporarily the temperature of the muscle. This can be shown in large animals by inserting a thermometer between the thigh muscles and stimulating the spinal cord. The rise of temperature may amount to several degrees.

In the case of frog's muscles, Helmholtz found that, after tetanising them for two or three minutes, the temperature rises 0·14° to 0·18° C.; and for each single twitch Heidenhain gives a rise of temperature of from 0·001° to 0·005° C.

For the detection of such small rises in temperature, a *thermopile*, and not a thermometer, is employed.

A thermopile consists of a junction of two different metals; the metals are connected by wires to a galvanometer. If the junction is heated an electrical current passes round the circuit, and is detected by the galvanometer. The metals usually employed are iron and German silver, or antimony and bismuth. If the number of couples in the circuit is increased, each is affected in the same way, and thus the electrical current is increased through the galvanometer. The arrangement is shown in the fig. 178, which also indicates the direction of the currents produced, the metals employed being antimony and bismuth. By using 16 couples of this kind Helmholtz was able to detect a change of $\frac{1}{4000}$ of a degree Centigrade.

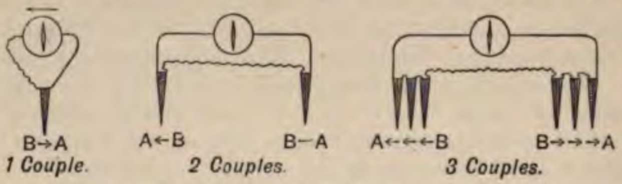

FIG. 178.—Scheme of thermo-electric couples. (After Waller.)

Within certain limits, the strength of the current is directly proportional to the rise of temperature at the junction.

If two couples are in circuit, as shown in the second diagram, and they are heated equally, no current will pass through the galvanometer, the current through one couple being opposed by the current through the other. But if the two couples are heated unequally, the direction of swing of the galvanometer needle indicates which is the warmer. To apply this to the frog's gastrocnemius, plunge several needle-shaped couples (diagram 3) into a frog's gastrocnemius of one side and the same number of couples into the gastrocnemius of the other side, and then excite first one then the other sciatic nerve; a deflection of the galvanometer will be observed first in one, then in the other direction, indicating the production of heat first on one side, then on the other.

Chemical Changes in Muscles.

The chemical changes which are normally occurring in a resting muscle are much increased when it contracts. Waste products of oxidation are discharged, and the most abundant of these is carbonic acid. Sarco-lactic acid is also produced, and the alkaline reaction of a normal muscle is replaced by an acid one. The muscles of animals hunted to death are acid; the acid reaction to litmus paper of a frog's gastrocnemius can be readily shown after it has been tetanised for 10 to 15 minutes.

The quantity of oxygen consumed is increased, but the consumption of oxygen will not account for the much greater increase in the discharge of carbonic acid. This is illustrated by the following table:—

Venous Blood.	O, less than Arterial Blood.	CO_2 more than Arterial Blood.
Of resting muscle .	9 per cent.	6·71 per cent.
Of active muscle .	12·26 per cent.	10·79 per cent.

Indeed, a muscle can be made to contract and give off oxidation products like carbonic acid in an atmosphere containing no oxygen at all. The oxygen used is thus stored up in the muscle previously. The oxygen is not, however, present in the free state, for no oxygen can be detected in the gases obtained from muscles by means of an air-pump. Hermann has supposed that the oxygen enters into the formation of a complex hypothetical compound he calls *inogen*. On contraction he considers this is broken up into carbonic acid, sarco-lactic acid, and a proteid residue of myosin.

There are other chemical changes in the muscle when it contracts —namely, a change of glycogen into sugar, and an increase of nitrogenous waste. The question whether urea is increased during muscular activity is, however, a much debated one, and we shall return to it when we are studying the urine. What is certain is that the increased consumption of carbon (possibly in large measure derived from the carbohydrate stored in the muscle) is a much more marked and immediate feature than an increase in the consumption of nitrogen.

Fatigue.

If the nerve of a nerve-muscle preparation is continually stimulated, the muscular contractions become more prolonged (see p. 117), smaller in extent, and finally cease altogether.

The muscle is said to be fatigued: this is due to the consumption of the substances available for the supply of energy in the muscle, but more particularly to the accumulation of waste products of contraction; of these, sarco-lactic acid is probably an important one. Fatigue may be artificially induced in a muscle by feeding it on a weak solution of lactic acid, and then removed by washing out the muscle with salt solution containing a minute trace of an alkali. If the muscle is left to itself in the body, the blood-stream washes away the accumulation of acid products, and fatigue passes off.

The question next presents itself, where is the seat of fatigue? Is it in the nerve, the muscle, or the end-plates? If, after fatigue has ensued and excitation of the nerve of the preparation produces no more contractions, the muscle is itself stimulated, it contracts; this shows it is still irritable, and, therefore, not to any great extent the seat of fatigue.

If an animal is poisoned with curare, and it is kept alive by artificial respiration, excitation of a motor nerve produces no contraction of the muscles it supplies. If one goes on stimulating the nerve for many hours, until the effect of the curare has disappeared, the block at the end-plates* is removed and the muscles contract: the seat of exhaustion is therefore not in the nerves.

By a process of exclusion it has thus been localised in the nerve-endings.

When the muscle is fatigued in the intact body, there is, however, another factor to be considered beyond the mere local poisoning of the end-plates. This is the effect of the products of contraction passing into the circulation and poisoning the central nervous system. It is a matter of common experience that one's mental state influences markedly the onset of fatigue and the amount of muscular work one can do. This aspect of the question has been specially studied by Waller and by Mosso. Mosso devised an instrument called the *ergograph*, which is a modification of Waller's *dynamograph* invented many years previously. The arm, hand, and all the fingers but one are fixed in a suitable holder; the free finger repeatedly lifts a weight over a pulley, and the height to which it is raised is registered by a marker on a blackened surface.

By the use of this and similar instruments it has been shown that the state of the brain and central nervous system generally is a most important factor in fatigue, and that the fatigue products produced in the muscles during work cause most of their injurious effects by acting on the central nervous system and diminishing its power of sending out impulses.

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* Another convenient block which is sometimes used is to throw a constant current into the nerve between the point of excitation and the muscles. This prevents the nerve impulses from reaching the muscles.

One of the most striking of Mosso's experiments illustrates in a very forcible manner the fact that the central nervous system is more easily fatigued than the nerve-endings in muscle. A person goes on lifting the weight until, under the influence of the will, he is unable to raise it any more. If then without waiting for fatigue to pass off, the nerves going to the finger muscles are stimulated artificially by induction shocks, they once more enter into vigorous contraction.

Mosso has also shown that the introduction of the blood of a fatigued animal into the circulation of a normal one will give rise in the latter to all the symptoms of fatigue. The blood of the fatigued animal contains the products of activity of its muscles, but still remains alkaline; the poisonous substance cannot therefore be free lactic acid; and lactates do not produce the effect. Lactic acid is doubtless one only of the products of muscular activity; we have at present no accurate knowledge of the chemical nature of the others.

The statement that nerves are not fatiguable, does not mean that the nerve fibres undergo no metabolic changes when transmitting a nerve impulse, but that the change is so slight, and the possibilities of repair so great, that fatigue in the usual acceptation of the term cannot be demonstrated. Waller made the interesting but tentative suggestion that the medullary sheath is a great factor in repair, or, in his own words, "the active grey axis both lays down and uses up its own fatty sheath, and it is inexhaustible not because there is little or no expenditure, but because there is an ample re-supply."

A year or two after these words were written, Miss Sowton, at Dr Waller's suggestion, undertook a piece of work in order to test the truth of this hypothesis. If the absence of fatigue is due to the presence of the fatty sheath, fatigue ought to be demonstrable in nerve-fibres in which the fatty sheath is absent. She selected the olfactory nerve of the pike as the non-medullated nerve with which to try the experiment, and her results confirmed Dr Waller's expectation; the galvanometric replies of the nerve become somewhat feebler after repeated stimulation.

It appeared to me advisable to test the question in another way. The splenic nerves seemed to be the most convenient large bundles of non-medullated fibres for the purpose. Dr T. G. Brodie was associated with me in carrying out the investigation. A dog is anæsthetised, the abdomen opened, the spleen exposed, and the splenic nerves which lie by the side of the main splenic artery are laid bare. It is quite easy to dissect out a length of nerve sufficient for the experiment (1½ to 2 inches). The nerve is then cut as far from the spleen as possible, and the spleen is enclosed in an air oncometer connected to the bellows volume recorder invented by Dr Brodie. On stimulating the nerve with a weak faradic current the organ contracts, and the recording lever falls. The diminution of the size of the spleen is quite visible to the naked eye, however, without the use of any apparatus. The next thing to do is to put a block on the course of the nerve, which will prevent the nerve impulses from reaching the spleen. Here we met with some difficulty. Curare and atropine are both ineffective: the constant current has a great disadvantage; non-medullated nerves are so much affected that very feeble constant currents will completely block the transmission of impulses, and not only that, but the nerve remains blocked after the current is removed. After the current has been allowed to flow for two minutes the nerve remains impassable to nerve impulses for an hour or more, and then slowly recovers. If, therefore, faradic excitation of the nerve is kept up all this time and fails to excite the contraction of the spleen after the removal of the constant current, it is impossible to say whether this is due to fatigue of the nerve-fibres on the proximal side of the block, or whether it may not be due to the fact that the block created by the constant current is still effective.

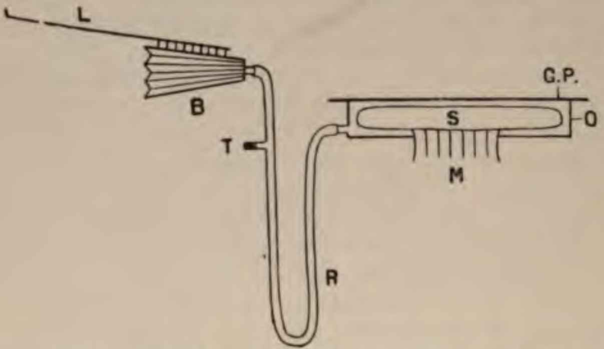

FIG. 179.—Apparatus for obtaining splenic curves. S, spleen in oncometer O, which is made of gutta-percha, and covered with a glass plate (G.P.) luted on with vaseline. M, is the splenic mesentery containing vessels and nerves; this passes through a slit in the base of the oncometer which is made air-tight with vaseline. The oncometer is connected to the flexible bellows (B) by the india-rubber tube (R), the side tube (T) being closed during an experiment by a piece of glass rod. The recording lever (L) writes on a revolving drum.

Our best results were obtained by using cold instead of a constant current as our blocking agent.

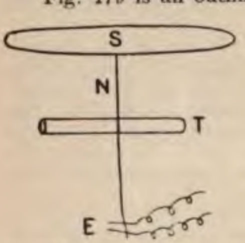

FIG. 180.—Arrangement of apparatus in connection with the splenic nerve. S is the spleen, and N the main bundle of nerves. The nerve rests on the metal tube (T) through which fluid at the required temperature is kept flowing, and on the electrodes (E) which come from the secondary coil of an inductorium.

Fig. 179 is an outline drawing of the apparatus used, and fig. 180 shows the arrangement adopted in connection with the nerve. The nerve (N) rests on a metal tube (T) through which water can be kept flowing. E is the situation of the electrodes. If the nerve is excited, the spleen contracts, and the recording lever (in fig. 179) falls. If now brine at 0 to 2° C. is kept flowing through T, the nerve impulses are blocked by the cold, and cannot reach the spleen. Immediately the cold brine is replaced by warm water at 30° C., the nerve again becomes passable by nerve impulses, and the spleen contracts once more.

If while the fluid in T is kept at the low temperature mentioned, the nerve is being excited with strong induction shocks all the time, the spleen remains irresponsive; the nerve impulses are able to reach T but not to pass it. If then warm water is passed through T, and the block produced by the cold is thus removed, and the spleen continues to be irresponsive, we have a proof that the piece of nerve between E and T has been fatigued. But our experiments have shown us that non-medullated nerve is just as difficult to fatigue as medullated nerve. Even after six hours' continuous excitation the nerve is just as excitable as it was at the start, and a full splenic contraction is obtained when the cold block is removed.

We have made similar experiments with vaso-motor nerves, such as the cervical sympathetic nerve in the rabbit, the splanchnic nerve of the dog, and the sciatic nerve in a curarised dog, and have obtained corresponding results. This confirms the work previously published by Eve. Eve excited the cervical sympathetic for twelve hours, and found no loss of excitability at the end of that time. Eve stimulated the nerve below the upper cervical ganglion, and the main object of his work was to ascertain whether any histological evidence of fatigue could be found in the cells of the ganglion. The only change he could find there was a somewhat diffuse staining of the cells by methylene blue, which he attributes to the formation of acid substances in the cells. A blue stain of similar appearance may be induced in the motor cells of the spinal cord, after exhaustion is produced in them by giving strychnine. In such experiments the spinal cord becomes as a rule distinctly acid to litmus paper. Max Verworn has more recently employed strychnine as a means of producing fatigue. He considers that the only specific effect of this alkaloid is increase of reflex activity, and he attributes the subsequent paralysis to vascular conditions and the accumulation of fatigue products, among which he places carbon dioxide in the first rank. Eve, on the contrary, did not find that carbonic acid alone produces the effects.

We must conclude from such experiments that Dr Waller's theory is unproved, and that while fatigue is demonstrable in nerve-cells, it has never yet been shown to occur in nerve-fibres of either the medullated or non-medullated variety.

In carrying out these experiments we noticed that though no functional fatigue can be demonstrated, there is noticeable, especially in vaso-motor nerves, a phenomenon which Howell terms *stimulation fatigue*; this means that the actual spot of nerve stimulated becomes after a time less excitable, and finally, inexcitable, though it will still transmit impulses, if the excitation is applied above the spot originally stimulated. We think that the use of the term "fatigue" in this connection is a mistake; the prolonged electrical excitation causes injurious polarisation (due to electrolytic changes) of the nerve, which renders it less excitable. This view has been confirmed by Prof. Gotch by means of experiments with the capillary electrometer. This so-called "stimulation fatigue" was not excluded in Miss Sowton's experiments, and will possibly explain her results. The splenic nerves, curiously enough, do not exhibit this phenomenon in any marked degree, and so were peculiarly well adapted to test the question of functional fatigue. On *à priori* grounds we should hardly expect non-medullated nerves to be peculiarly susceptible of real fatigue, when one considers how many of them, like the vaso-constrictors, are in constant action throughout life.

Rigor Mortis.

After death, the muscles gradually lose their irritability and pass into a contracted condition. This affects all the muscles of the body, and usually fixes it in the natural posture of equilibrium or rest. The general stiffening thus produced constitutes *rigor mortis* or *post-mortem* rigidity.

The cause of rigor is the coagulation of the muscle-plasma, which is more fully described in the next section. This coagulation results in the formation of *myosin*, and is gradual in onset. Simultaneously the muscles (a) *become shortened and opaque*, (b) *heat is evolved*, (c) *they give off carbonic acid*, and (d) *become acid in reaction*; this is due in part to the formation of sarco-lactic acid, and in part to the formation of acid phosphates.

After a varying interval, the rigor passes off, and the muscles are once more relaxed. This sometimes occurs too quickly to be caused by putrefaction, and the suggestion that in such cases at any rate such relaxation is due to a ferment-action is very plausible. It is known that a pepsin-like or proteolytic ferment is present in muscle, as in many other animal tissues, kidney, spleen, etc. (Hedin), and that such ferments act best in an acid medium. The conditions for the solution of the coagulated myosin are therefore present, as the reaction of rigored muscle is acid.

Order of Occurrence.—The muscles are not affected simultaneously by rigor mortis. It affects the neck and lower jaw first; next, the upper extremities, extending from above downwards; and lastly, reaches the lower limbs; in some rare instances it affects the lower extremities before, or simultaneously with, the upper extremities. It usually ceases in the order in which it begins: first at the head, then in the upper extremities, and lastly in the lower extremities. It seldom commences earlier than ten minutes, or later than seven hours after death; and its duration is greater in proportion to the lateness of its accession.

The occurrence of rigor mortis is not prevented by the previous existence of paralysis in a part, provided the paralysis has not been attended with very imperfect nutrition of the muscular tissue.

In some cases of sudden death from lightning, violent injuries, or paroxysms of passion, rigor mortis has been said not to occur at all; but this is not always the case. It may, indeed, be doubted whether there is really a complete absence of the post-mortem rigidity in any such cases; for the experiments of Brown-Séquard make it probable that the rigidity may supervene immediately after death, and then pass away with such rapidity as to be scarcely observable.

Chemical Composition of Muscle.

The phenomena of rigor mortis will be more intelligible if we consider the chemical composition of muscle.

The connective tissue of muscle resembles connective tissue elsewhere; the gelatin and fat obtained in analyses of muscle are derived from this tissue. The sarcolemma is composed of a substance which resembles elastin in its solubilities.

The contractile substance within the muscular fibres is, during life, of semi-liquid consistency, and contains a large percentage of proteids and smaller quantities of extractives and inorganic salts. By the use of a press this substance can be squeezed out of perfectly fresh muscles, and it is then called the *muscle-plasma.*

After death, muscle-plasma, like blood-plasma, coagulates (thus causing the stiffening known as *rigor mortis*). The solid clot corresponding to the fibrin from blood-plasma is called *myosin*, and the liquid residue is called the *muscle-serum.*

Pursuing the analogy further, it is found that the coagulation of both muscle-plasma and blood-plasma can be prevented by cold, by strong solutions of neutral salts, and by potassium oxalate, which precipitates, as the insoluble oxalate of calcium, the lime salts essential for the coagulation process. In both cases the clotting is produced by the action of a ferment developed after death. In both cases the precursor of the solid clot is a proteid of the globulin class which previously existed in solution.

Fibrin in the blood-clot is formed from the previously soluble fibrinogen of the blood-plasma. Myosin in the muscle-clot is formed from the previously soluble *myosinogen*[*] of the muscle-plasma. When the blood-clot contracts it squeezes out blood-serum; when the muscle-clot contracts it squeezes out muscle-serum. The muscle-serum contains small quantities of albuminous material, together with the extractives and salts of the muscle. The origin of the sarco-lactic acid is a controversial question: some believe it originates from the carbohydrate (glycogen and sugar); others think it comes from the proteid molecules in the muscle.

The general composition of muscular tissue is the following:—

Water	75	per cent.
Solids	25	„
Proteids	18	„
Gelatin	2 to 5	„
Fat		
Extractives	0·5	„
Inorganic salts	1 to 2	„

The proteids, as already stated, chiefly pass into the clot: very little is found in the muscle-serum.

The extractives comprise a large number of organic substances, all present in small quantities, some of which are nitrogenous, like creatine, creatinine, xanthine, and hypoxanthine: the rest are non-nitrogenous—namely, fats, glycogen, sugar, inosite, and the variety of lactic acid known as sarco-lactic acid. The inorganic salts are chiefly salts of potassium, especially potassium phosphate.

The condition of dead muscle reminds one somewhat of contracted muscle. Indeed, the similarity is so striking that Hermann has propounded the idea that contracted muscle is muscle on the road to death, the differences between the two being of degree only. He considers that, on contraction, *inogen* (see p. 149) is broken up into carbonic acid, sarco-lactic acid, and myosin; on death the same change occurs, only to a much more marked extent.

This idea is a far-fetched one, but it is a useful reminder of the similarities of the two cases. In chemical condition, contracted and dead muscle are alike, so far as the formation of acid products is concerned; there is, however, no evidence of any formation of a muscle-clot (myosin) during the contraction of living muscle, as there is in dead muscle. Then heat is produced in both cases, and in both cases also the muscle is electro-positive to uncontracted muscle.

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[*] For further details see small text at the end of this chapter.

Here, however, the analogy must end: for living contracted muscle is irritable, dead muscle is not. Living contracted muscle is more extensible than uncontracted muscle; muscle in *rigor mortis* is not so (see fig. 156, p. 128). The contraction of living muscle is favoured by feeding it with a solution of dextrose, while the process of *rigor* is hindered by the same solution. (F. S. Lee.)

Our correct knowledge of the proteids of muscle and of the phenomena of *rigor mortis* date from the year 1864, when Kühne obtained muscle-plasma by subjecting frozen frog's muscle to strong pressure. A good many years later I was successful in repeating these experiments with mammalian muscle. By fractional heat coagulation, and by their varying solubilities in neutral salts, I was able to separate four different proteids in the muscle-plasma.

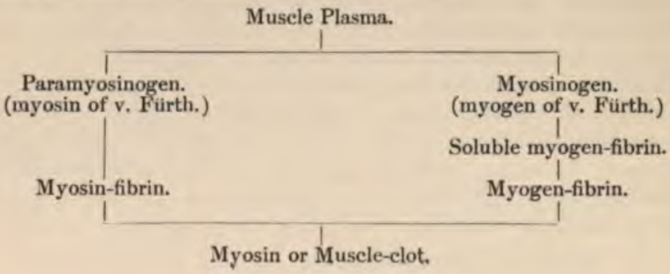
1. A globulin precipitable by heat at 47° C. This is analogous to the cell-globulin found in most protoplasmic structures. I gave it the name *paramyosinogen*.
2. A proteid with many of the characters of a globulin, coagulable by heat at 56° C.; and this I termed *myosinogen*.
3. A globulin (*myo-globulin*), precipitable by heat at 63° C.
4. An albumin similar in its properties to serum albumin is also present; but this and the myo-globulin only occur in quite small amounts.

In addition to these, there is a small quantity of nuclei-proteid from the nuclei, and in the red muscles hæmoglobin is present; the normal pigment of the so-called pale muscles is termed *myo-hæmatin* by MacMunn, and this is doubtless a derivative of hæmoglobin.

The two most abundant and important proteids are the first two in the list, namely, paramyosinogen and myosinogen. They occur in the proportion of about 1 to 4, and both enter into the formation of the muscle-clot (myosin). The myo-globulin is possibly not a separate proteid, but only some myosinogen which has escaped coagulation: the albumin is probably derived from adherent blood and lymph.

In 1895 v. Fürth took up the subject. On the main question we are in substantial agreement, namely, that in the muscle-plasma there are the two proteids just alluded to, and that these both contribute to the formation of the muscle-clot. The main points of difference between us are in the names of the proteids. He uses physiological saline solution to extract the muscle-plasma, and this extract coagulates spontaneously on standing; he is doubtful whether a specific myosin-ferment brings about the change. Paramyosinogen he terms *myosin*, and this passes directly into the clotted condition (*myosin-fibrin*); but myosinogen, called *myogen* by v. Fürth, first passes into a soluble condition (coagulable by heat at the remarkably low temperature of 40° C.) before it clots: the soluble stage he calls *soluble myogen-fibrin*, and the clot *myogen-fibrin*.

We may put this in a diagrammatic way as follows:—



V. Fürth also calls attention to some characters of myosinogen which separate it from the typical globulins; *e.g.*, it is not precipitable by dialysing the salts away from its solutions. It may be therefore called an *atypical* globulin.

In mammalian muscle, soluble myogen-fibrin is only found as a stage in the process of *rigor mortis*, but in the muscles of the frog and other amphibia it is present as such in the living muscle.

The muscle-plasma from fishes' muscle contains another proteid termed *myoproteid* by v. Fürth. It is precipitable by dialysis, but not coagulable by heat.

Brodie, and later, Vernon, did some interesting experiments on *heat rigor*. When a muscle is heated above a certain temperature it becomes contracted and stiff, losing its irritability completely. This is due to the coagulation of the muscle proteids. If a tracing is taken of the contraction, it is found to occur in a series of steps: the first step in the shortening occurs at the coagulation temperature of the paramyosinogen (47°-50° C.), and if the heating is continued, a second shortening occurs at 56° C., the coagulation temperature of myosinogen. If, however, a frog's muscle is used, there are three steps, namely, at 40° (coagulation temperature of soluble myogen-fibrin), 47°, and 56°. This work of Brodie's is especially valuable because it teaches us that the proteids in muscle-plasma, or in saline extracts of muscle, are present also in the actual muscle-substance. He also made clear another important point, namely, that the irritability of the muscle is lost after the *first* step in the shortening has occurred. In other words, in order to destroy the vitality of muscular tissue, it is not necessary to raise the temperature sufficiently high to coagulate all its proteids, but that when one of the muscular proteids has been coagulated, the living substance as such is destroyed; the proteids of muscle cannot therefore be regarded as independent units; the unit is protoplasm, and if one of its essential constituents is destroyed, protoplasm as such ceases to live.

Hans Przibram has attempted to classify the animal kingdom on the basis of the muscle-proteids; his conclusions are based on the examination of only thirty species of animals, and may require revision in the future, but such as they are, they are as follows:—

Invertebrates: para-myosinogen present; myosinogen absent.

Vertebrates: para-myosinogen and myosinogen both present.

Fishes: in addition to these two principal proteids, soluble myogen-fibrin and myoproteid (in large quantities) occur.

Amphibians: like fishes, except that myoproteid is only present in traces.

Reptiles, birds, mammals: myoproteid is absent, and soluble myogen-fibrin is only present when *rigor mortis* commences.

Steyrer has recently stated that on prolonged tetanisation (in rabbits' muscle) the amount of paramyosinogen diminishes, but when degeneration occurs after the motor nerves are cut, the amount of this proteid increases. Such results must, however, be accepted with caution until more satisfactory methods than those at present in use are adopted for the estimation of the muscle-proteids.

CHAPTER XIV

COMPARISON OF VOLUNTARY AND INVOLUNTARY MUSCLE

THE main difference between voluntary and involuntary muscle is the difference expressed in their names. Voluntary muscle is under the control of that portion of the central nervous system the activity of which is accompanied by volition. Involuntary muscle, on the other hand, is, as a rule, also under the control of the central nervous system, but of a portion of the central nervous system the activity of which is independent of volition. There appear, however, to be exceptions to this rule, and the involuntary muscle executes its contractions independently of nervous control; that is to say, it is sometimes in the truest sense of the term really involuntary. This is very markedly seen in the developing heart of the embryo, which begins to beat before any nerve fibres have grown into it from the central nervous system.

Another characteristic of involuntary muscle is a tendency to regular alternate periods of rest and activity, or *rhythmicality*. This is best exemplified in the heart, but it is also seen in the lymphatic vessels, especially the lymph hearts of the frog, and the mesenteric lymphatic vessels (lacteals) of many animals. It is seen in the veins of the bat's wing, and in the muscular tissue of the spleen, stomach, intestine, bladder, and other parts.

A third characteristic of involuntary muscle is *peristalsis*. If any point of a tube of smooth muscle such as the small intestine is stimulated, a ring-like constriction is produced at this point. After lasting some time at this spot it slowly passes along the tube at the rate of 20 to 30 millimetres per second. This advancing peristaltic wave normally takes place in only one direction, and so serves to drive on the contents of the tube.

Involuntary muscle nearly always contains numerous plexuses of non-medullated nerve-fibres with ganglion cells; so that much discussion has taken place on the question whether the phenomena of rhythmicality and peristalsis are properties of the muscular tissue itself or of the nerves mixed with it. The evidence available (namely, that portions of muscular tissue entirely free from nerves act in the same way as those that possess nerves) indicates that it is the muscular rather than the nervous tissues that possess these properties; though it can hardly be doubted that under usual circumstances the contraction of involuntary muscle is influenced and controlled by nervous agency.

The artificial stimuli employed for smooth muscle are the same as those used for striated muscle; single induction shocks are often ineffectual to produce contraction, but the make, and to a less extent the break, of a constant current will act as a stimulus.

The faradic current is a good stimulus, but it never throws involuntary muscle into tetanus; in the heart, strong stimulation will sometimes effect a partial fusion of the beats, but never complete tetanus. The rate of stimulation makes no difference; in fact, very often a rapid rate of stimulation calls forth less rapidly occurring contractions than a slow rate.

A stimulus strong enough to produce a contraction in the heart elicits a maximum contraction ("all or nothing" Waller); the phenomenon known as the *staircase* (see p. 117) is generally better marked in the case of the heart than in that of voluntary muscle.

The contraction of smooth muscle is so sluggish that the various stages of latent period, shortening and relaxation, can be followed with the eye; the latent period often exceeds half a second in duration. It does not obey the "all or nothing" law.

The normal contraction of voluntary muscle is a kind of tetanus (see p. 121); the normal contraction of cardiac and plain muscle is a much prolonged single contraction. A very valuable piece of evidence in this direction is seen in the experiment on the heart with the physiological rheoscope (see p. 145). Each time the heart contracts the rheoscopic preparation executes a single twitch, not a tetanus. This is an indication that the electrical change is a single one, and not a succession of changes such as occurs in tetanus.

When this electrical change is examined with the electrometer, it is seen that it is a diphasic one as in voluntary muscle; but in a slowly contracting tissue like the heart-muscle the two phases are separated by a prolonged period of equipotentiality, and thus they are rendered more distinct. The illustrations already given (figs. 167 and 168) show this fact graphically.

When the heart is beating sluggishly in the rheoscopic experiment above referred to, the separation of the two phases of the electrical change will sometimes cause two twitches in the muscle-nerve preparation. Bayliss and Starling describe the ventricular contraction of the mammalian heart as being accompanied by a triphasic electrical variation; this is due to the contraction at the base outlasting that at the apex; if, therefore, base and apex are led off to the electrometer, the first phase is due to increased positivity at the base, the second to that at the apex; this quickly subsides, but the increased positivity at the base which still continues accounts for the third excursion of the mercury.

But though involuntary muscle cannot be thrown into tetanus, it has the property of entering into a condition of sustained contraction called *tonus*. We shall have to consider this question again in connection with the plain muscular tissue of the arterioles.

Involuntary muscle when it contracts undergoes thermal and chemical changes similar to those we have dealt with in the case of the voluntary muscles.

Involuntary muscle is usually supplied with two sets of nerves, one of which (accelerator) increases and the other of which (inhibitory) decreases its activity. The nerve-endings in involuntary muscle require a much larger dose of curare to affect them than the end-plates in voluntary muscle.

The phenomena of *rigor mortis* in involuntary muscle have not been so fully studied as in the case of voluntary muscle. It has, however, been shown that the chemical composition of involuntary muscle differs in no noteworthy manner from that of voluntary muscle, and on death the muscle becomes acid; such products as carbonic acid and sarco-lactic acid are formed. In the heart, stomach, uterus, and rectum, *post-mortem* rigidity has been noted, and it probably occurs in all varieties of plain muscle.

Swale Vincent has shown that the characteristic proteids (paramyosinogen and myosinogen) occur in both striped and unstriped muscle, and the heat rigor curves of involuntary muscle are practically identical with those obtained by Brodie (see p. 157). He is inclined to think that the two proteids are formed by the breaking down of a compound proteid which in living muscle mainly coagulates at 47° C. This view is taken by Stewart in reference to striped muscle also, but has been very seriously questioned by v. Fürth. The most striking chemical difference between unstriped and striped muscle is seen in the amount of nucleo-proteid which they contain. Plain muscle contains six to eight times the amount found in voluntary muscle; cardiac muscle contains an intermediate quantity.

CHAPTER XV

PHYSIOLOGY OF NERVE

MANY points relating to the physiology of nerve have been already studied in connection with muscle. But there still remain further questions upon which we have hardly touched as yet.

Classification of Nerves.

The nerve-fibres which form the conducting portions of the nervous system may be classified into three main groups, according to the direction in which they normally conduct nerve impulses. These three classes are:—

1. Efferent nerve-fibres.
2. Afferent nerve-fibres.
3. Inter-central nerve-fibres.

1. **Efferent** or *centrifugal* nerves are those which conduct impulses from the central nervous system (brain and spinal cord) to other parts of the body. When, for instance, there is a wish to move the hand, the impulse starts in the brain, and travels a certain distance down the spinal cord; it leaves the spinal cord by one or more of the spinal nerves, and so reaches the muscles of the hand which are thrown into contraction. Such nerves are called *motor*, but all efferent nerves are not motor; some cause secretion instead of movement, and others may cause a stoppage of movement, etc. A list of the classes of efferent nerves is as follows:—

a. Motor.
b. Accelerator.
c. Inhibitory.
d. Secretory.
e. Electrical.
f. Trophic.

a. Motor nerves. Some of these go to voluntary muscles; others to involuntary muscles, such as the vaso-motor nerves which supply the muscular tissue in the walls of arteries.

b. *Accelerator* nerves are those which produce an increase in the rate of rhythmical action. An instance of these is seen in the sympathetic nerves that supply the heart.

c. *Inhibitory* nerves are those which cause a slowing in the rate of rhythmical action, or it may be its complete cessation. Inhibitory nerves are found supplying many kinds of involuntary muscle; a very typical instance is found in the inhibitory fibres of the heart which are contained within the trunk of the vagus nerve.*

d. *Secretory* nerves are found supplying many secreting glands, such as the salivary glands, pancreas, gastric glands, and sweat glands. The impulse which travels down a secretory nerve stimulates secretion in the gland it supplies.

e. *Electrical* nerves are found in the few fishes which possess electrical organs. The impulse which travels down these nerves causes the electrical organ to be thrown into activity.

f. *Trophic* nerves are those which control the nutrition of the part they supply.

2. **Afferent** or *centripetal* nerves are those which conduct impulses in the reverse direction, namely, from all parts of the body to the central nervous system. When one feels pain in the finger, the nerves of the finger are stimulated, an impulse travels up the nerves to the spinal cord, and then to the brain. The mental process set up in the brain is called a sensation; the sensation, however, is referred to the end of the nerve where the impulse started, and the sensation of pain does not appear to occur in the brain, but in the finger. This is an instance of a sensory nerve; and the terms afferent and sensory may often be used synonymously. The nerves of sensation may be grouped as follows:—

a. The nerves of special sense; that is, of sight, hearing, taste, smell, and touch.

b. The nerves of general sensibility; that is, of a vague kind of sensation not referable to any of the special senses just enumerated; as an instance, we may take the vague feelings of comfort or discomfort in the interior of the body.

c. Nerves of pain. It is a moot point whether these are anatomically distinct from the others, for any excessive stimulation of a sensory nerve whether of the special or general kind will cause pain.

The words "sensory" and "afferent," however, are not quite synonymous. Just as we may have efferent impulses leaving the brain for the heart or blood-vessels of which we have no conscious knowledge, so also afferent impulses may travel to the central nervous system which excite no conscious feelings. The afferent nerve-tracts to the cerebellum form a very good instance of these.

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* The question has been much debated whether voluntary muscle is provided with inhibitory nerves; they do, however, appear to be present in certain nerves supplying the muscles of the claws of lobsters and similar crustaceans.

Then, too, the excitation of many afferent nerves will excite what are called reflex actions. We are very often conscious of the sensations that form the cause of a reflex action, but we do not necessarily have such sensations. Many reflex actions, for instance, occur during sleep; many may be executed by the spinal cord even after it has been severed from the brain, and so the brain cannot be aware of what is occurring.

A reflex action is an action which is the result of an afferent impulse. Thus a speck of dust falls into the eye, and causes movements of the eyelids to get rid of the offending object. The dust excites the sensory nerve-endings in the conjunctiva, an impulse travels to the centre of this nerve in the brain, and from the brain a reflected impulse travels to the muscles of the eyelid. As an instance of a reflex action in which secretion is concerned, take the watering of the mouth which occurs when food is seen or smelt. The nerves of sight or smell convey an afferent impulse to the brain, which reflects, down the secretory nerves, an impulse which excites the salivary glands to activity.

These, however, are instances of reflex action which are accompanied with conscious sensation, but like all pure reflex actions are not under the control of the will.

An instance of a reflex action not accompanied with consciousness is seen in a man with his spinal cord cut across or crushed, so that any communication between his brain and his legs is impossible. He cannot move his legs voluntarily, and is unconscious of any feelings in them. Yet when the soles of his feet are tickled he draws his legs up, the centre of reflex action being in the grey matter of the lower region of the spinal cord.

For a reflex action, three things are necessary: (1) an afferent nerve, (2) a nerve-centre consisting of nerve-cells to receive the afferent impulse and send out an efferent impulse, and (3) an efferent nerve along which the efferent impulse may travel. If the reflex action is a movement, the afferent nerve is called *excito-motor;* if it is a secretion, the afferent nerve is called *excito-secretory;* and similarly, afferent nerves may also be *excito-accelerator, excito-inhibitory,* etc.

3. **Intercentral** nerves are those which connect nerve-centres together; they connect different parts of brain, and of the cord to one another, and we shall find in our study of the nerve-centres that they are complex in their arrangement.

Investigation of the Functions of a Nerve.

There are always two main experiments by which the function of a nerve may be ascertained. The first is *section*, the second is *stimulation*.

Section consists in cutting the nerve and observing the loss of function that ensues. Thus, if a motor nerve is cut, motion of the muscles it supplies can no longer be produced by activity of the nerve-centre; the muscle is paralysed. If a sensory nerve is cut, the result is loss of sensation in the part it comes from.

Stimulation of the cut nerve is the opposite experiment. When a nerve is cut across, one piece of it is still connected with the brain or spinal cord; this is called the *central end;* the other piece, called the *peripheral end*, is still connected with some peripheral part of the body. Both the central and the peripheral end should be stimulated; this is usually done by means of induction shocks. In the case of a motor nerve, stimulation of the central end produces no result; stimulation of the peripheral end produces a nervous impulse which excites the muscles to contract. In the case of a sensory nerve, stimulation of the peripheral end has no result, but stimulation of the central end causes a sensation, usually a painful one, and reflex actions, which are the result of the sensation.

When a nerve is cut across, there are other results than the loss of function just mentioned; for even though the nerve is still left within the body with a normal supply of blood, it becomes less and less irritable, till at last it ceases to respond to stimuli altogether. This diminution of excitability starts from the point of section and travels to the periphery, but is temporarily preceded by a wave of increased excitability travelling in the same direction (Ritter-Valli law).

This loss of excitability of nerve is accompanied with degenerative changes which are of so great importance as to demand a separate section.

Degeneration of Nerve.

Suppose a nerve is cut right across, the piece of the nerve left in connection with the brain or spinal cord remains healthy both in structure and functions; but the peripheral piece of the nerve loses its functions and undergoes what is generally called, after the discoverer of the process, *Wallerian degeneration*. A nerve is made up of nerve-fibres, and each nerve-fibre is essentially a branch of a nerve-cell; when the nerve is cut, the axis cylinders in the peripheral portion are separated from the cells of which they are branches and from which they have grown. These separated portions of the axis cylinders die, and the medullary sheath of each undergoes a gradual process of disintegration into droplets of myelin, which are ultimately absorbed and removed by the lymphatics. At the same time there is a multiplication of the nuclei of the primitive sheath. This degenerative process is evident two or three days after the section has been made. In the case of the non-medullated fibres, there is no medullary sheath to exhibit the disintegrative changes just alluded to; and the nuclei of the sheath do not multiply; there is simply death of the axis cylinder. The degeneration occurs simultaneously throughout the whole extent of the nerve; it does not start from the section and travel to the periphery. Ranvier's original diagram is reproduced in fig. 181. Figs. 182 and 183 are photo-micrographs from actual specimens.

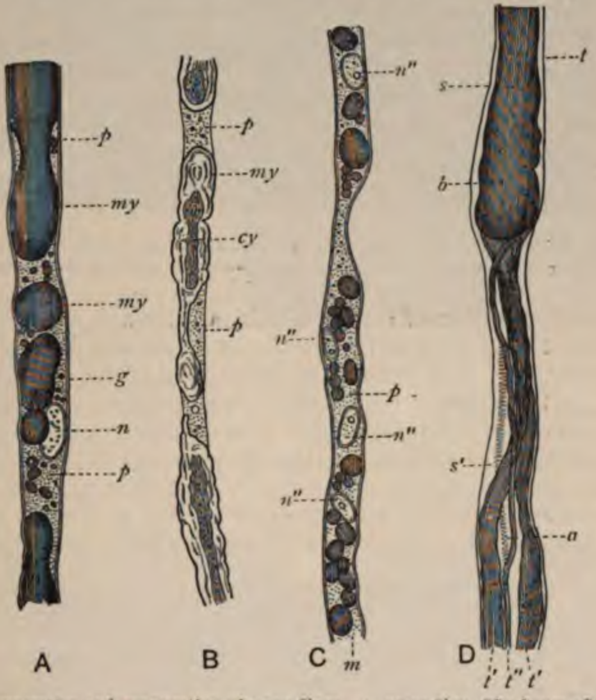

FIG. 181.—Degeneration and regeneration of nerve-fibres. A, nerve-fibre, fifty hours after operation. *my*, medullary sheath breaking up into myelin drops. *p*, granular protoplasm replacing myelin. *n*, nucleus. *g*, primitive sheath. B, nerve-fibre after four days. *cy*, axis cylinder partly broken up and enclosed in portions of myelin. C, a more advanced stage in which the medullary sheath has almost disappeared. Numerous nuclei, *n''*, are seen. D, commencing regeneration; several fibres (*t'*, *t''*) have sprouted from the somewhat bulbous cut end (*b*) of the nerve-fibre. *a*, an axis cylinder which has not yet acquired its medullary sheath. *s*, *s'*, primitive sheath of the original fibre. (Ranvier.)

A great amount of attention has been directed to this process of degeneration, because it has formed a valuable method of research in tracing nervous tracts, and ascertaining the nerve-cells from which they originate. It must not, however, be regarded as an isolated phenomenon in physiology; it is only an illustration of the universal truth that any portion of a cell (in this case the axis cylinder process) cut off from the nucleus of the cell degenerates and dies.

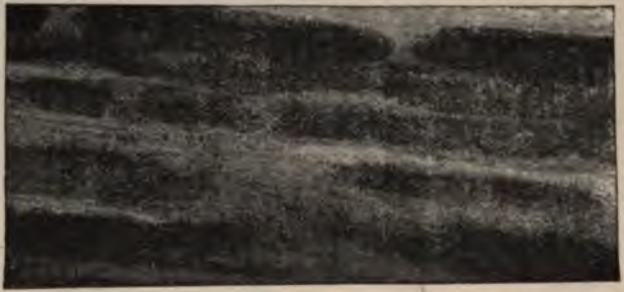

FIG. 182.—Nerve-fibres from sciatic nerve of cat, four days after the nerve had been cut. This shows an early stage of the degenerative process. 600 diameters. (Mott and Halliburton.)

If a nerve is simply cut, and allowed to heal, regeneration of function in time occurs. This is hastened by the surgeon suturing the cut ends of the nerve together. It must not, however, be supposed that this is due to a restoration of the structure of the fibres in the peripheral portion of the cut nerve. It is due to very fine new nerve-fibres sprouting out from the central end of the cut nerve, and growing distalwards. This is illustrated in D, fig. 181. When regeneration does not take place, the central ends of the cut fibres and the cells from which they originate undergo slow atrophic changes (*disuse atrophy*).

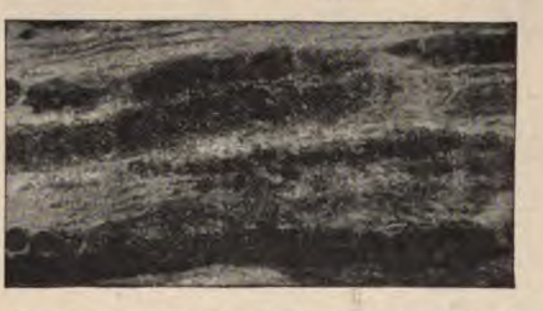

FIG. 183.—These are fibres from the sciatic nerve of another cat, ten days after the nerve had been cut. This shows the breaking-up of the medullary sheath in a marked way, and the intense black colour the myelin droplets take with osmic acid. 600 diameters. (Mott and Halliburton.)

The view expressed by the earlier workers on nerve regeneration that the new fibres grow from the central stump of the cut nerves has been recently questioned. Some believe that regeneration may occur in the peripheral structures. It certainly is the case that the neurilemmal cells exhibit a great deal of activity; they multiply (fig. 184); at a later stage they exhibit a phagocytic action in the removal of the degenerated fat (fig. 185); and later still they become elongated and spindle-shaped; they then join together as though they were forming the basis of new nerve-fibres (fig. 186). But the elongating and apparently contiguous cells are probably only forming a new sheath or basis into which the axis cylinder ultimately grows. Howell and Huber, who have recently investigated this question, have arrived at the conclusion that the peripheral structures are active in preparing the scaffolding, but that the axis cylinder, the essential portion of a nerve-fibre, has an

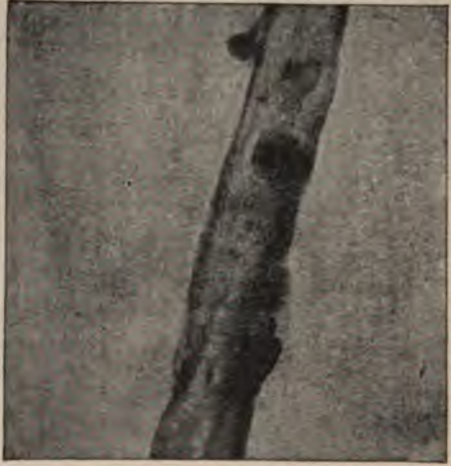

FIG. 184.—Single fibre from a degenerating nerve, eight days after the nerve was cut, stained so as to show the division of a neurilemmal nucleus into two. 870 diameters. (Mott and Halliburton.)

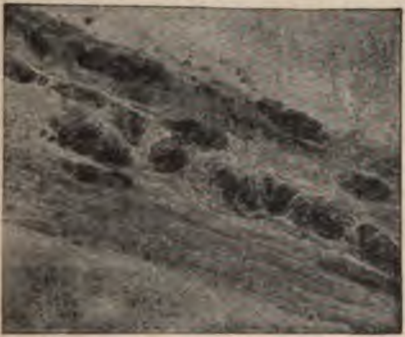

FIG. 185.—Degenerated nerve, twenty-seven days after the nerve had been cut. The numerous neurilemmal cells, perhaps aided by phagocytes from the exterior contain within them fatty particles which stain black with osmic acid. They are doubtless active in removing the degenerated myelin. 450 diameters. (Mott and Halliburton.)

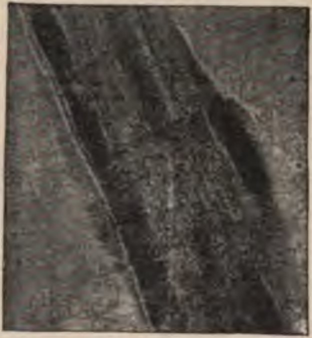

FIG. 186.—Degenerated nerve forty-four days after section. The elongation of the neurilemmal cells to form what look like new fibres is well shown. 500 diameters. (Mott and Halliburton.)

exclusively central origin. This view I thoroughly endorse. Mott and I have also shown that when the regenerated fibres are again cut, degeneration takes place in the peripheral direction only, and this is a strong piece of evidence that growth had not started from the periphery centralwards, for the direction of nutritive control is always the direction of growth.

The manifest activity of the neurilemmal cells is probably largely nutritive rather than formative, but is nevertheless of great importance, for, in situations like the central nervous system, where the neurilemma does not exist, regeneration does not occur.

Functions of the Roots of the Spinal Nerves.

The general truths enunciated in the two preceding sections are well illustrated by the experiments made to determine the functions of the roots of the spinal nerves. Each spinal nerve originates from the spinal cord by two roots. One of these is called the *anterior* or *ventral* root: it consists of nerve-fibres which originate from the large multipolar cells in that portion of the grey matter in the interior of the spinal cord which we shall presently learn to call the anterior horn. These nerve-fibres are all medullated; the large ones join up with the posterior root to form the spinal nerve; the small nerve-fibres leave the root and pass to the sympathetic chain, which then distributes non-medullated fibres to the involuntary muscular fibres of the blood-vessels and viscera.

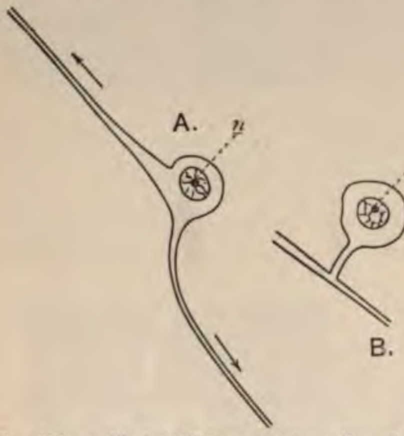

Fig. 187.—A, Bipolar cell from spinal ganglion of a 4½ weeks embryo. n, nucleus; the arrows indicate the direction in which the nerve processes grow, one to the spinal cord, the other to the periphery. B, a cell from the spinal ganglion of the adult; the two processes have coalesced to form a T-shaped junction. (Diagrammatic.)

The other root, *the posterior* or *dorsal* root, has upon it a collection of nerve-cells forming the spinal ganglion. Each nerve-cell is enclosed within a nucleated sheath of connective tissue origin, and it is from these nerve-cells that the fibres of the posterior roots grow. In the embryo, each nerve-cell has two processes (fig. 187), one of which grows to the spinal cord, where it terminates by branching around the multipolar cells of the grey matter; the other process grows outwards to the periphery. In the adult mammal (not in fishes) the two processes coalesce in the first part of their course, forming a *T-shaped junction.*

The first experiments on the functions of the spinal nerve-roots were performed in this country by Sir Charles Bell (1811), and in France by Magendie (1822). These observers found that on section of the anterior roots there resulted paralysis of the muscles supplied by the nerves; on section of the posterior roots there was loss of sensation. These experiments clearly pointed to the conclusion that the anterior roots contain the efferent (motor) fibres; and the posterior roots the afferent (sensory) fibres. This conclusion was confirmed by the experiment of stimulation. Stimulation of the peripheral end of the cut anterior root caused muscular movement; of the central end, no effect. Stimulation of the central end of the cut posterior root caused pain and reflex movements; of the peripheral end, no effect.

Recurrent sensibility.—One of the statements just made requires a slight modification; namely, excitation of the peripheral end of a divided anterior root will evoke pain and reflex movements, as well as direct movements; that is to say, the anterior root, though composed mainly of motor fibres, contains a few sensory fibres coming probably from the membranes of the spinal cord, and then running into the posterior root with the rest of the sensory fibres. They often, however, run down the mixed nerve a considerable distance before returning to the posterior roots.

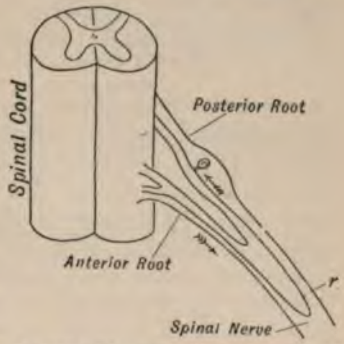

FIG. 188.—Diagram to illustrate recurrent sensibility.

The diagram on this page (fig. 188) illustrates the course of one of these recurrent fibres (r); the arrows represent the direction in which it conveys impulses.

Degeneration of roots.—The facts in connection with this subject were made out by Waller (1850), and may be best understood by referring to the next diagram (fig. 189).

A represents a section of the mixed nerve beyond the union of the roots; the whole nerve beyond the section degenerates, and is shaded black.

B represents the result of section of the anterior root; only the anterior root-fibres degenerate; the sensory fibres of the posterior root remain intact. The small medullated nerve-fibres (not shown in the diagram) also degenerate as far as the ganglion cells of the sympathetic system with which they communicate. The recurrent sensory fibres in this root do not degenerate with the others, but are found degenerated in the part of the anterior root attached to the spinal cord.

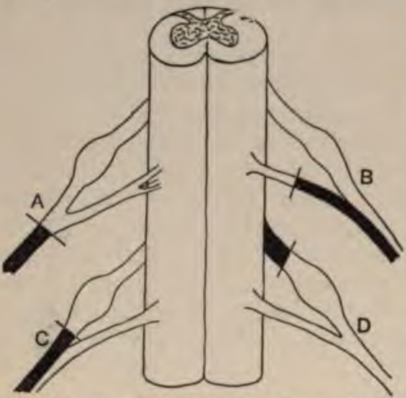

FIG. 189.—Diagram to illustrate Wallerian degeneration of nerve-roots.

Section of the posterior root always produces the same physiological effect (loss of sensation)* wherever the section is made, but the degeneration effect is different according as the section is made on the proximal or distal side of the ganglion. If the section is made beyond the ganglion, the degeneration occurs as shown in C beyond the section in the peripheral portion of the posterior root-fibres; the anterior root remains intact except for the recurrent sensory fibres which it contains. If the section is made as in D, between the ganglion and the cord, the only piece that degenerates is the piece severed from the ganglion and running into the cord; these fibres may be traced up in the posterior column of the spinal cord until they terminate in grey matter, which they do at different levels. The whole of the sensory fibres including the recurrent ones which are still attached to the ganglion remain histologically healthy.

The accompanying figure (fig. 190) is one of the original illustrations made by Dr Waller, and I am indebted to the present Dr Waller for permission to reproduce it.

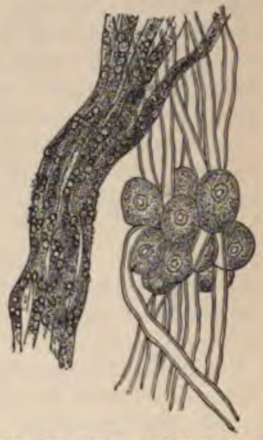

FIG. 190.—Groups of fibres from the anterior and posterior roots several days after section of both roots close to the cord; the anterior fibres are degenerated; the posterior, being still in connection with the nerve-cells from which they grew, are normal.

These facts of degeneration teach us, what we also learn from the study of embryology, that the nerve-fibres of the anterior root are connected to the nerve-cells within the spinal cord, while the posterior root-fibres are connected to the cells of the spinal ganglia; or, to put it another way, the trophic centres which control the nutrition of the nerve-fibres are situated within the cord for the anterior roots, and within the spinal ganglia for the posterior roots.

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* In order to obtain any appreciable loss of motion or sensation, it is necessary to divide several roots (anterior or posterior as the case may be) as there is a good deal of overlapping in the peripheral distribution of the fibres.

Changes in a Nerve during Activity.

When a nerve is stimulated, the change produced in it is called a nervous impulse; this change travels along the nerve, and the propagation of some change is evident from the effects which follow: sensation, movement, secretion, etc.; but in the nerve itself very little change can be detected. There is no change in form; the most delicate thermo-piles have failed to detect any production of heat, and we are also ignorant of any chemical changes. The only alteration which can be detected as evidence of this molecular change in a nerve is the electrical one. Healthy nerve is iso-electric, but during the passage of a nervous impulse along it there is a very rapid diphasic variation, which travels at the same rate as the nervous impulse. This is similar to the diphasic change in muscle, which we have already studied, and can be detected in the same way.

Waller regards the current of action of any excitable tissue as an index of the magnitude of action, and records the movement of the galvanometer by photographing the excursion of the spot of light on a moving photographic plate. He has in this way obtained records from muscle, nerve, retina, skin, plant tissues, etc. He points out that the only available index of action within the nerve itself is the electrical sign of activity, whereas in muscle the mechanical action can be compared with its accompanying electrical changes. The amount of contraction *in a muscle* caused by excitation of its nerve is only a very rough, or even a fallacious, indication of the excitability *of the nerve*, because the nerve is connected to the muscle by motor end-plates, and these, as we have already seen, are fatigued long before the nerve shows any sign of fatigue.

Using this method, Waller has obtained a number of interesting results on the variation in nerve action produced by drugs and other agents. He finds that the effect of carbonic acid is to cause a diminution, and finally disappearance of the galvanometric response; when this gas is replaced by air the nerve recovers, and the action-currents increase. Ether acts similarly; but with chloroform recovery is difficult to obtain. Small doses of carbonic acid increase the action-currents, and Waller considers that the staircase effect in muscle (p. 117), and the similar progressive increase noted in the action-currents of nerve as the result of repeated stimulation are due to the evolution of this gas during activity.

This hypothesis has been recently confirmed by some experiments of Bæyer and Fröhlich. They have shown that peripheral nerves participate in respiratory exchanges, using up oxygen and producing carbonic acid in measurable amounts.

There can be no doubt that the existence of the electrical variation is as a rule the index of the excitatory alteration in a nerve. In the isolated nerve it is in fact the only change that can be detected. But in the present state of our knowledge we are not justified in assuming that it gives an absolutely faithful record. The electrical variation can be detected in a nerve for many days after its removal from the body. Although the electrical change is a concomitant of the real excitatory process, the former may be therefore perceptible when other evidence of the existence of the latter fails. Moreover, Gotch and Burch have obtained further evidence of the dissociation of the electrical response from the excitatory process. In the frog's sciatic nerve, it is possible with two stimuli in rapid succession to obtain only one electrical response near the seat of excitation which has been cooled, while two such responses occur in a more peripheral warmer region.

Excitability and conductivity.—It is necessary to distinguish between these two properties of nerve. Changes in excitability, and in the power of conducting nerve impulses, do not necessarily go together, as shown in the following experiment:—The nerve of a frog's leg is led through a glass tube, the ends of which are sealed with clay, care being taken that the nerve is not compressed. The tube is provided with an inlet and outlet, so that gases may be passed through it. Two pairs of electrodes are arranged, so that the nerve can be stimulated either within or outside the little gas chamber. If carbon dioxide or ether vapour is passed through the tube, both excitability and conductivity are in time abolished, but excitability disappears first; at this stage, if the nerve is stimulated by an induction shock inside the tube, the muscle does not respond, but on stimulating the nerve at the end distant from the muscle and outside the tube, the muscle contracts. The nerve, therefore, is not excitable, though it will conduct impulses. At a later stage shocks administered by either pair of electrodes provoke no contraction. When the poisonous vapour is replaced by air, the nerve recovers, and conductivity returns before excitability. If alcohol vapour is used conductivity is stated to vanish before excitability.

Gotch has shown that cold applied to a nerve acts very much like carbonic acid. Intense cold will cause disappearance of both excitability and conductivity; but cold of such a degree which abolishes the excitability of the nerve to induction shocks, increases its excitability to the constant current, and also to mechanical and thermal stimuli.

Velocity of a Nerve Impulse.

A nervous impulse is not electricity; compared to that of electricity its rate of propagation is extremely slow. It has been measured in motor nerves as follows: a muscle-nerve preparation is made with as long a nerve as possible; the nerve is stimulated first as near to the muscle, and then as far from the muscle, as possible. The moment of stimulation and the moment of commencing contraction is measured by taking muscle tracings on a rapidly moving surface in the usual way, with a time-tracing beneath. The contraction ensues later, when the nerve is stimulated at a distance from the muscle, than in the other case, and the difference in the two cases gives the time occupied in the passage of the impulse along the piece of nerve, the length of which can be easily measured.

A similar experiment can be performed on man by means of the transmission myograph (see p. 122). If a tracing of the contraction of the thumb muscles is taken, the two stimuli may be successively applied through the moistened skin, first at the brachial plexus below the clavicle; and secondly, at the median nerve at the bend of the elbow.

Another method, largely employed by Bernstein, is to take the electrical change as the indication of the impulse. The rheotome is the instrument used. If fig. 169 (p. 139) is referred to, and a long nerve substituted for the muscle-nerve preparation, the stimulus is applied at one end, and the change in the electrical condition of the nerve is recorded by the galvanometer, which is connected to the other end of the nerve. The time measurement is effected by the adjustment of the rheotome, which must be such as to tap off the electrical change at the moment it occurs.

The rate of the transmission of nervous impulses discovered by these methods is, in a frog's motor nerve, 28 to 30 metres a second; in human motor nerves, 33 metres a second; in sensory nerves, 30 to 33 metres a second.

Direction of a Nerve Impulse.

Nerve impulses are conducted normally in only one direction: in efferent nerves from, in afferent nerves to, the nerve-centres. But there are some experiments which point to the conduction occurring under certain circumstances in both directions.

Thus, in the rheotome experiment just described, if the nerve is stimulated in the middle instead of at one end, the electrical change (the evidence of an impulse) is found to be conducted towards both ends of the nerve.

Kühne's gracilis experiment proves the same point. The gracilis muscle of the frog (fig. 191) is in two portions, with a tendinous intersection, and supplied by nerve-fibres that branch into two bundles; excitation strictly limited to one of these bundles, after division of the tendinous intersection, causes both portions of the muscle to contract.

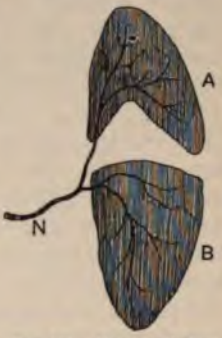

FIG. 191.—Gracilis of frog. (After Waller.)

Another striking experiment of the same kind can be performed with the nerve that supplies the electrical organ of Malapterurus. This nerve consists of a single axis cylinder and its branches; stimulation of its posterior free end causes the "discharge" of the electrical organ, although the nervous impulse normally travels in the opposite direction.

Crossing of Nerves.

Some experiments designed to prove the possibility of nervous conduction in both directions were performed many years ago by Paul Bert. He grafted the tip of a rat's tail either to the back of the same rat, or to the nose of another. When union had been effected, the tail was amputated near its base. After a time, irritation of the end of the trunk-like appendage on the back or nose of the rat gave rise to sensation. The impulse thus passed from base to tip, instead of from tip to base, as formerly. This experiment does not, however, prove the point at all; for all the original nerve-fibres in the tail must have degenerated, and the restoration of sensation was due to new fibres, which had grown into the tail. Exactly the same objection holds to another series of experiments, in which the motor and sensory nerves of the tongue were divided and united crosswise. Restoration of both movement and sensation does occur, but is owing to new nerve-fibres growing out from the central stumps of the cut nerves.

Though these experiments do not prove what they were intended to, they are of considerable interest in themselves. Dr R. Kennedy has recently carried out a very careful piece of work on this question of nerve crossing. He cut in a dog's thigh the nerves supplying the flexor and the extensor muscles, and sutured them together crosswise. Regeneration of structure and restoration of function occurred equally quickly, as in those cases in which the central ends had been united to the peripheral ends of their own proper nerves. On examining the cortex of the brain in those animals in which nerve-crossing had been accomplished, it was found that stimulation of the region which in a normal animal gave flexion, now gave extension of the limb, and *vice versâ*.

A series of equally important experiments have more recently been carried out by Langley, in which he shows that the same facts are true for the nerves that supply involuntary muscle. These nerve-fibres will under certain experimental conditions terminate by arborising around other nerve-cells than those which they normally form connections (synapses) * with. It will be sufficient to give one typical experiment. If the vagus nerve is cut across in the neck, its peripheral end degenerates downwards; if the cervical sympathetic is cut across below the superior cervical ganglion, its peripheral end degenerates upwards, as far as the ganglion. If subsequently the central end of the cut vagus is united to the peripheral end of the cut sympathetic, in the course of some weeks the vagus fibres grow into the sympathetic and form synapses around the cells of the superior cervical ganglion, and stimulation of the united nerve now produces such effects as are usually obtained when the cervical sympathetic is irritated; for instance, dilatation of the pupil, raising of the upper eyelid, and constriction of blood-vessels of the head and neck. (See accompanying diagram, fig. 192).

Such experiments as these are important because they teach us that though the action of nerves may be so different in different cases (some being motor, some inhibitory, some secretory, some sensory, etc.), after all what occurs in the nerve trunk itself is always the same; the difference of action is due to difference either in the origin or distribution of the nerve-fibres. If we remember the familiar illustration in which nerve trunks are compared to telegraph wires, we may be helped in realising this. The destination of a certain group of telegraph wires may be altered, and the alteration may produce different consequences at different places; the electric change, however, in the wires would be the same in all cases. So the nerve impulse going along a nerve is always the same sort of molecular disturbance; if it is made as in the experiment just described, to go by a wrong channel, it produces just the same results as though the impulse had reached its destination by the usual channel.

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* The meaning of the term "synapse" is fully explained in Chapter XVII. (p. 198).

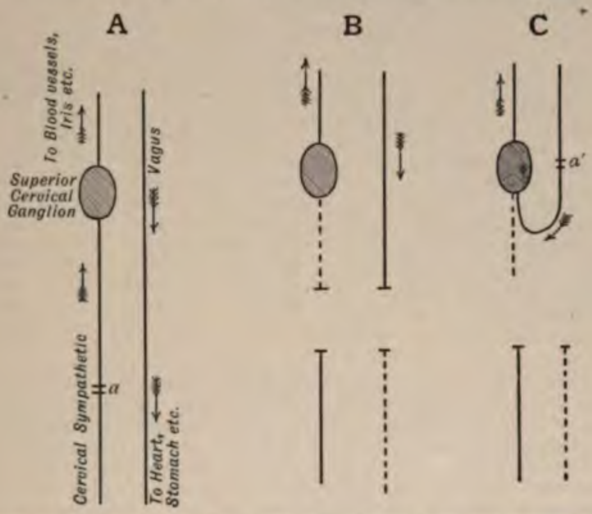

FIG. 192.—Diagram to illustrate Langley's experiment on vagus and cervical sympathetic nerves. In A, the two nerves are shown intact; the direction of the impulses they normally carry is shown by arrows, and the names of some of the parts they supply are mentioned. In B, both nerves are cut through. The degenerated portions are represented by discontinuous lines. In C, the union described in the text has been accomplished, and stimulation at the point a' now produces the same results as were in the intact nerves (A) produced by stimulation at a.

Chemistry of Nervous Tissues.

The following table gives some typical analyses of the solids of nervous tissues, but these tissues also contain a large amount of water; this is present in larger

Portion of Nervous System.	Proteids.	Lecithin.	Cholesterin and Fat.	Cerebrin.	Neurokeratin.	Other Organic matters.	Salts.
Grey matter of Brain	55	17	19	0·5	6·7		1·5
White matter of Brain	25	10	52	9·5	3·3		0·6
Spinal Cord	23	75·1					1·1
Human Sciatic Nerve	36	32	12	11	3	4	—

amount (83 per cent.) in grey matter than in white matter (70 per cent.); in early than in adult life; in the brain than in the spinal cord; in the spinal cord than in nerves.

One should next note the high percentage of proteid. In grey matter, where the cells are prominent structures, this is most marked, and of the solids, proteid material here comprises more than half of the total. The following are some of my analyses which give the mean of a number of observations on the nervous tissues of human beings, monkeys, dogs, and cats:

	Water.	Solids.	Percentage of Proteids in Solids.
Cerebral grey matter . .	83·5	16·5	51
,, white ,, . .	69·9	30·1	33
Cerebellum	79·8	20·2	42
Spinal cord as a whole .	71·6	28·4	31
Cervical cord . . .	72·5	27·5	31
Dorsal cord . . .	69·8	30·2	28
Lumbar cord . . .	72·6	27·4	33
Sciatic nerves . . .	65·1	34·9	29

The most abundant proteid is *nucleo-proteid;* there is also a certain amount of *globulin*, which, like the paramyosinogen of muscle, is coagulated by heat at the low temperature of 47° C. A certain small amount of neurokeratin (especially abundant in white matter) is included in the above table with the proteids. The granules in nerve cells (Nissl's bodies), which stain readily with methylene blue, are nucleo-proteid in nature. The next most abundant substances are of a fatty nature; the most prominent of these is the phosphorised fat called *lecithin*. In the nervous tissues some of the lecithin is combined with cerebrin to form a complex substance called *protagon*, which crystallises out on cooling a hot alcoholic extract of brain or other nervous structures. *Cerebrin* is a term which probably includes several substances, which are nitrogenous glucosides; they yield on hydrolysis the sugar called galactose. They are sometimes called cerebrosides. *Kephalin* is another phosphorised fat which is present. The crystalline monatomic alcohol *cholesterin* is also a fairly abundant constituent of nervous structures, especially of the white substance of Schwann. Finally, there are smaller quantities of other extractives and a small proportion of mineral salts (about 1 per cent. of the solids).

In connection with the substances just enumerated, it is necessary to enter a little more fully into the composition of lecithin. An ordinary fat contains the elements carbon, hydrogen, and oxygen, and when it takes up water it is split or hydrolysed into its constituent parts, glycerin and fatty acid.

Fat + water.

Glycerin. Fatty acid.

Lecithin ($C_{42}H_{84}NPO_9$) contains not only carbon, hydrogen, and oxygen, but nitrogen and phosphorus as well. When it is hydrolysed, it yields not only glycerin and a fatty acid, but also phosphoric acid, and a nitrogenous base termed choline.

Lecithin + water.

Glycerin. Fatty acid. Phosphoric acid. Choline.

Fresh nervous tissues are alkaline, but, like most other living structures, they turn acid after death. The change is particularly rapid in grey matter. The acidity is due to lactic acid.

Little or nothing is known of the chemical changes nervous tissues undergo during activity. We know that oxygen is very essential, especially for the activity of grey matter; cerebral anæmia is rapidly followed by loss of consciousness and death. We have already seen that similar respiratory exchanges, though less in amount, are stated to occur in peripheral nerves (see p. 171).

Chemistry of nerve degeneration.—Mott and I have shown that in the disease General Paralysis of the Insane, the marked degeneration that occurs in the brain is accompanied by the passing of the products of degeneration into the cerebro-spinal fluid. Of these, nucleo-proteid and choline—a decomposition product of the lecithin—are those which can be most readily detected. Choline can also be found in the blood. But this is not peculiar to the disease just mentioned, for in various other degenerative nervous diseases (combined sclerosis, disseminated sclerosis, meningitis, alcoholic neuritis, beri-beri, etc.) choline can also be detected in these situations. The tests employed to detect choline are mainly two: (1) a chemical test, namely, the obtaining of the characteristic yellow octahedral crystals of the platinum double salt from the alcoholic extract of the cerebro-spinal fluid or blood;[*] (2) a physiological test, namely, the lowering of arterial blood-pressure (partly cardiac in origin, and partly due to dilatation of peripheral vessels) which a saline solution of the residue of the alcoholic extract produces: this fall is abolished, or even replaced by a rise of arterial pressure, if the animal has been poisoned with atropine. It is possible that such tests may be of diagnostic value in the distinction between organic and so-called functional diseases of the nervous system. The chemical test can frequently be obtained with 10 c.c. of blood, or even less.

A similar condition can be produced artificially in animals by a division of large nerve trunks; and is most marked in those animals in which the degenerative process is at its height as tested histologically by the Marchi reaction.[†] A series of cats was taken, both sciatic nerves divided, and the animals subsequently killed at intervals varying from 1 to 106 days. The nerves remain practically normal as long as they remain irritable, that is up to 3 days after the operation. They then show a progressive increase in the percentage of water, and a progressive decrease in the percentage of phosphorus until degeneration is complete. When regeneration occurs, the nerves return approximately to their previous chemical condition. When the Marchi reaction disappears in the later stages of degeneration, the non-phosphorised fat has been absorbed. This absorption occurs earlier in the peripheral nerves than in the central nervous system.

Further, it has been found that in spinal cords in which a unilateral degeneration of the pyramidal tract has been produced by a lesion in the opposite hemisphere, there is a similar increase of water and diminution of phosphorus on the degenerated side.

The following table shows these main results in the experiments on cats just described.

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[*] This test is performed as follows: the fluid is diluted with about five times its volume of alcohol and the precipitated proteids are filtered off. The filtrate is evaporated to dryness at 40° C. and the residue dissolved in absolute alcohol and filtered; the filtrate from this is again evaporated to dryness, and again dissolved in absolute alcohol, and this should be again repeated. To the final alcoholic solution an alcoholic solution of platinum chloride is added, and the precipitate so formed is allowed to settle and washed with absolute alcohol by decantation; the precipitate is then dissolved in 15-per-cent. alcohol, filtered, and the filtrate is allowed to slowly evaporate in a watch-glass at 40° C. The crystals can then be seen with the microscope. They are recognised not only by their yellow colour and octahedral form, but by their solubility in water and 15-per-cent. alcohol, but also by the fact that on incineration they yield 31 per cent. of platinum and give off the odour of trimethylamine.

[†] The Marchi reaction is the black staining that the medullary sheath of degenerated nerve-fibres shows when, after being hardened in Müller's fluid, they are treated with Marchi's reagent, a mixture of Müller's fluid and osmic acid. Healthy nerve-fibres are not affected by the reagent, but normal adipose tissue is blackened like degenerated myelin. The osmic acid reaction is due to fats like olein. which belong to the acrylic series.

Cat's sciatic nerves.					
	Water.	Solids.	Percentage of phosphorus in solids.	Condition of blood.	Condition of nerves.
Normal	65·1	34·9	1·1	Minimal traces of choline present.	Nerves irritable and histologically healthy.
1 to 3 days after section	64·5	35·5	0·9		
4 to 6 ,,	69·3	30·7	0·9	Choline more abundant.	Irritability lost; degeneration beginning.
8 ,,	68·2	31·8	0·5	Choline abundant.	Degeneration well shown by Marchi reaction.
10 ,,	70·7	29·3	0·3		
13 ,,	71·3	28·7	0·2		
25 to 27 ,,	72·1	27·9	traces	Choline much less.	Marchi reaction still seen, but absorption of degenerated fat has set in.
29 ,,	72·5	27·5	0		
44 ,,	72·6	27·4	0	Choline almost disappeared.	Absorption of fat practically complete.
100 to 106 ,,	66·2	3·8	0·9	Choline almost disappeared.	Return of function, nerves regenerated.

The above figures relate to the peripheral portions of the nerves. Noll has shown that the phosphorised material protagon also diminishes somewhat in the central ends of cut nerves due to "disuse atrophy."

Heat contraction of nerve.—A nerve, when heated, shortens; this shortening occurs in a series of steps which, as in the case of muscle, take place at the coagulation temperatures of the proteids present. The first step in the shortening occurs in the frog at about 40°, in the mammal at about 47°, and in the bird at about 52° C. The nerve is killed at the same temperatures.

Cerebro-spinal fluid.—This plays the part of the lymph of the central nervous system, but differs considerably from all other forms of lymph. It is a very watery fluid, containing, besides some inorganic salts similar to those of the blood, a trace of proteid matter (globulin) and a small amount of sugar. It contains the merest trace of choline; but this is not devoid of significance, for this fact taken in conjunction with another—namely, that physiological saline solution will extract from perfectly fresh nervous matter a small quantity of choline—shows us that lecithin and protagon are not stable substances, but are constantly breaking down and building themselves up afresh; in fact, undergoing the process called metabolism. This is most marked in the most active region of the brain—viz., the grey matter.

CHAPTER XVI

ELECTROTONUS

WHEN a constant current is thrown into a nerve, there is an excitation which leads to a nervous impulse, and this produces a contraction of the muscle at the end of the nerve. Similarly, there is another contraction when the current is taken out. While the current is flowing through the nerve, the muscle is quiescent. But while the current is flowing there are changes in the nerve, both as regards its electrical condition and its excitability. These changes are summed up in the expression *electrotonus.*

In the investigation of this subject the instruments employed are the same as those already described, with the addition of two others that it will be convenient to describe before passing on to the study of electrotonus itself. These are the reverser or commutator, and the rheochord.

Pohl's commutator is the form of reverser generally employed. It consists of a block of ebonite provided with six pools of mercury, each of which is provided with a binding screw. The corner pools are connected by diagonal cross wires, and by a cradle consisting of an insulating handle fixed to two arcs of copper wire which can be tilted so that the two middle pools can be brought into communication with either of the two lateral pairs of pools. Fig. 193 shows how, by

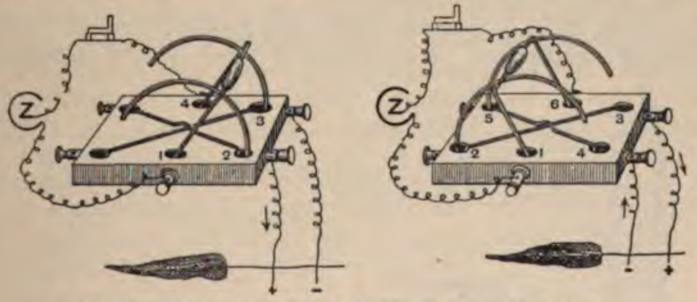

FIG. 193.—Pohl's Commutator, with cross wires. (After Waller.)

altering the position of the cradle, the direction of the current from one electrode to the other is reversed. The numbers 1, 2, 3, etc., indicate the path of the current in the two cases.

Sometimes the reverser is used without the cross wires for a different purpose. The battery wires are connected as before with the middle mercury pools. Each lateral pair of pools is connected by wires to a pair of electrodes. The two pairs of electrodes may be applied to two portions of a nerve, or to two different nerves, and by tilting the cradle to right or left the current can be sent through one or the other pair of electrodes.

The rheochord is an instrument by means of which the strength of a constant current passed through a nerve may be varied. It consists of a long wire (*r*, *r*, *r*) of high resistance stretched on a board. This is placed as a bridge on the course of the battery current. (See fig. 194.) The current is thus divided into two parts: one part through the bridge, the other through the nerve, which is laid across the two non-polarisable electrodes at the ends of the wires. The resistance through the bridge is varied by the position of the slider (*s s*). The farther the slider is from the battery end of the instrument the longer is the bridge, and the higher its resistance, so that less current goes that way and more to the nerve.

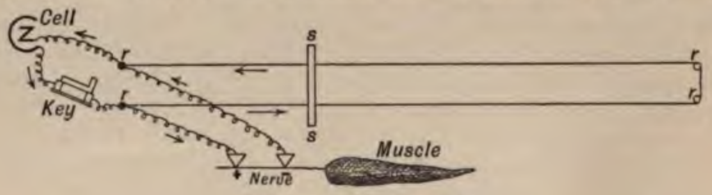

FIG. 194.—Simple Rheochord.

The next figure shows the more complicated form of rheochord invented by Poggendorf. The number of turns of wire is greater, so that the resistance can be varied to a much greater extent than in the simpler form of the instrument.

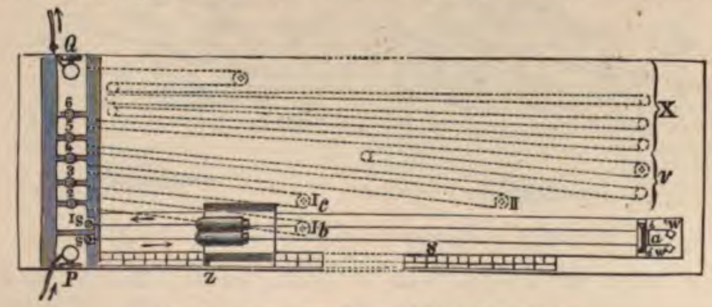

FIG. 195.—Poggendorf's Rheochord. (M'Kendrick.)

The term "electrotonus" includes two sets of changes in the nerve; first an electrical change, and secondly changes in excitability and conductivity. We will take the electrical change first.

Electrotonic currents.—The constant current is passed through the nerve from a battery, non-polarisable electrodes being used; it is called the polarising current. If portions of the nerve beyond the electrodes are connected ("led off") as in the diagram (fig. 196) by non-polarisable electrodes to galvanometers, a current will in each case be indicated by the swing of the galvanometer needles. The electrotonic current in the neighbourhood of the negative pole or kathode is called the *katelectrotonic current;* and that in the neighbourhood of the anode is called the *anelectrotonic current.* In both cases the electrotonic current has the same direction as the polarising current. These currents are dependent on the physical integrity of medullated nerve; they are not found in muscle, tendon, or non-medullated nerve; they are absent or diminished in dead or degenerated nerve. They can, however, be very successfully imitated in a model made of zinc wire encased in cotton soaked with salt solution. The electrotonic currents must be carefully distinguished from the normal current of action, which is a momentary change rapidly propagated with a nervous impulse which may be produced by any method of stimulation. The electrotonic currents are produced only by an electrical (polarising) current; they vary in intensity with the polarising current, and last as long as the polarising current passes through the nerve.

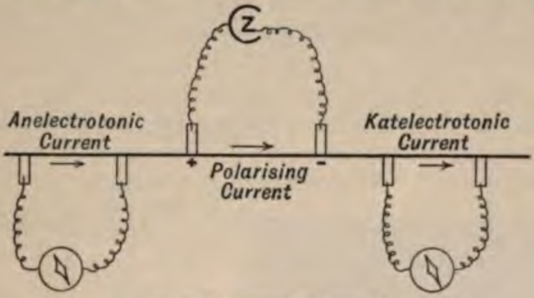

FIG. 196.—Electrotonic currents.

After the polarising current is removed, after-electrotonic currents occur in different directions in the three regions tested.

(*a*) In the intrapolar region, the after-current is opposite in direction to the original polarising current; unless the polarising current is strong and of short duration, when it is in the same direction.

(*b*) In the katelectrotonic region, the after-current has the same direction as the katelectrotonic current.

(*c*) In the anelectrotonic region, the after-current has at first the same, then the opposite direction to the anelectrotonic current.

The experiment known as the *paradoxical contraction* depends upon electrotonic currents. The sciatic nerve of the frog divides in the lower part of the thigh into two parts. If one division is cut across, and its central end stimulated *electrically* (the spinal cord having been previously destroyed), the muscles supplied by the other branch contract; the nerve-fibres in this branch having been stimulated by the electrotonic variation in the divided branch.*

Electrotonic alterations of excitability and conductivity.—When a constant current is passed through a nerve, the excitability and conductivity of the nerve are increased in the region of the kathode, and diminished in the region of the anode. When the current is taken out these properties are temporarily increased in the neighbourhood of the anode, and diminished in that of the kathode.

This may be shown in the case of a motor nerve by the following experiment. The next diagram represents the apparatus used.

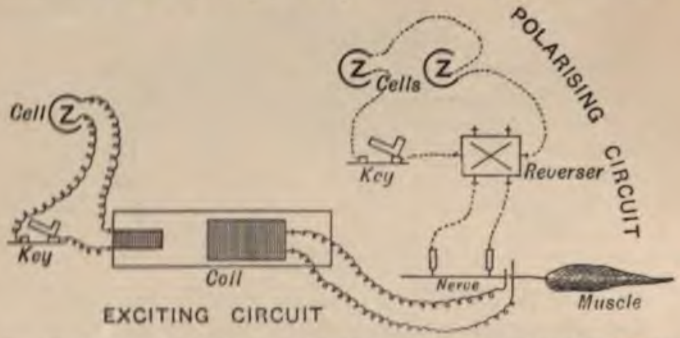

FIG. 107.—Diagram of apparatus used in testing electrotonic alterations of excitability.

An exciting circuit for single induction shocks is arranged in the usual way, the exciting electrodes being placed on the nerve near the muscle. A polarising circuit is also arranged, and includes a battery, key, and reverser; the current is passed into the nerve by means of non-polarisable electrodes. When the polarising current is thrown into the nerve, or taken out, a contraction of the muscle occurs, but these contractions may be disregarded for the present.

The exciting circuit is arranged with the secondary coil so far from the primary that the muscle responds to break only, and the tracing may be recorded on a stationary blackened cylinder. The cylinder is moved on a short distance, and this is repeated. The height of the lines drawn may be taken as a measure of the excitability of the nerve. The polarising current is then thrown in, in a *descending* direction (*i.e.*, towards the muscle); the kathode is thus the non-polarisable electrode near to the exciting electrodes. While the polarising current is flowing, take some more tracings by breaking the exciting current. The increase in the excitability of the nerve is shown by the much larger contractions of the muscle; probably a contraction will be obtained now at both make and break of the exciting current. After removing the polarising current, the contractions obtained by exciting the nerve will be for a short time smaller than the normal, but soon return to their original size.

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* This experiment must be carefully distinguished from Kühne's gracilis experiment described on p. 173. In the gracilis experiment the nerve-fibres themselves *branch*, and any form of stimulation applied to one branch will cause contraction of both halves of the muscle. In the paradoxical contraction, the bundles of nerve-fibres are merely bound *side by side* in the sciatic trunk; there is therefore no possibility of conduction of a nerve impulse in both directions; the stimulus, moreover, must be an electrical one.

Exactly the reverse occurs when the polarising current is *ascending*, *i.e.*, from the muscle towards the spinal cord. The non-polarisable electrode near the exciting electrodes is now the anode. While the polarising current is passing, the excitability of the nerve is diminished so that induction shocks which previously produced contractions of a certain size, now produce smaller contractions, or none at all. On removing the polarising current, the after-effect is increase of excitability.

The following figure is a reproduction of a tracing from an actual experiment. The after-effects are not shown. N represents a series of contractions obtained when the nerve is normal, K when it is katelectrotonic, A when it is anelectrotonic.

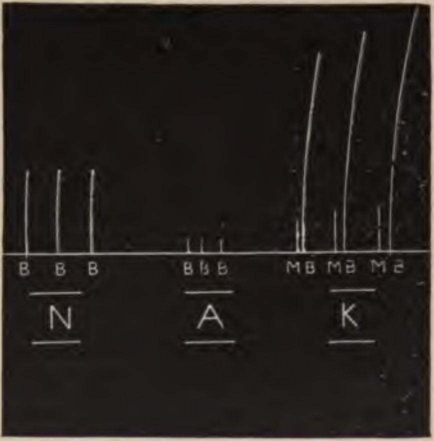

Fig. 198.—Electrotonus. M, make. B, break.

Exactly similar results are obtained if one uses mechanical stimuli, such as hammering the nerve, instead of induction shocks. The same is true for chemical stimuli. If the exciting electrodes are removed, and salt sprinkled on the nerve near the muscle, the latter soon begins to quiver; its contractions are increased by throwing in a descending and diminished by an ascending polarising current.

The increase in irritability is called **katelectrotonus,** and the decrease is called **anelectrotonus.** The accompanying diagram (fig. 199) shows how the effect is most intense at the points (*a* *k*) where the electrodes are applied, and extends in gradually diminishing intensity on each side of them. Between the electrodes the increase shades off into the decrease, and it is evident that there must be a *neutral point* where there is neither increase nor decrease of irritability. The position of this neutral point is found to vary with the intensity of the polarising current—when the current is weak the point is nearer the anode, when strong nearer the kathode.

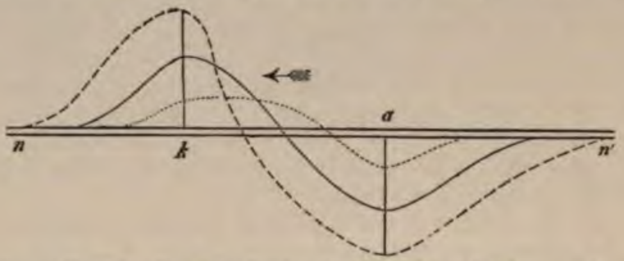

FIG. 199.—Diagram illustrating the effects of various intensities of the polarising current. *n*, *n'*, nerve; *a*, anode; *k*, kathode; the curves above indicate increase, and those below decrease of irritability, and when the current is small the increase and decrease are both small, with the neutral point near *a*, and as the current is increased in strength, the changes in irritability are greater, and the neutral point approaches *k*.

Pflüger's law of contraction.—The constant current sometimes causes a contraction both at make and break, sometimes at make only, sometimes at break only. The difference depends on the strength and direction of the current; and follows from the electrotonic changes of excitability and conductivity we have been studying. Increase of excitability acts as a stimulus; so that at the make the kathode is the stimulating electrode, and at the break the anode is the stimulating electrode.

The facts may be demonstrated in the following way (fig. 200): from a battery lead the wires to the middle screws of a reverser (with cross wires), interposing a key; from one pair of end screws of the reverser lead wires to the binding screws of the rheochord; from these same screws of the rheochord the non-polarisable electrodes lead to the nerve of a nerve-muscle preparation. The strength of the current is varied by the slider S. The nearer S is to the binding screws the

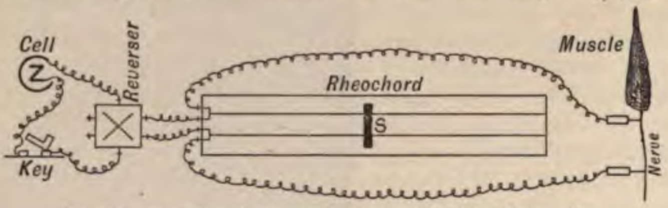

FIG. 200.—Arrangement of apparatus for demonstrating Pflüger's law.

less is the resistance in the rheochord circuit, and the less the current through the nerve. With a weak current, a contraction occurs at make only, but more readily, *i.e.* with a weaker current, when its direction is descending, *i.e.* towards the muscle. With a stronger current (ascending or descending) contraction occurs both at make and break. With a very strong current (six Groves), the contraction occurs only at make with a descending current; and only at break with an ascending current.

The contractions produced in the muscle of a nerve-muscle preparation by a constant current have been arranged in a table which is known as Pflüger's **Law of Contraction**.

STRENGTH OF CURRENT USED.	DESCENDING CURRENT.		ASCENDING CURRENT.	
	Make.	Break.	Make.	Break.
Weak . . .	Yes.	No.	Yes.	No.
Moderate . .	Yes.	Yes.	Yes.	Yes.
Strong . . .	Yes.	No.	No.	Yes.

The increase of irritability at the kathode when the current is made is greater, and so more potent to produce a contraction than the rise of irritability at the anode when the current is broken; and so with weak currents the only effect is a contraction at the make. But when the strength of the current is increased the rise of excitability is in all cases sufficient to provoke a contraction (moderate effect in above table). The alteration in conductivity is not sufficient to prevent the impulses being propagated to the muscle.

With strong currents the case is a little more complicated, because here the diminution of conductivity is so great that certain regions of the nerve become impassable by nerve impulses. When the current has an ascending direction, the impulse at the break is started at the anode, and as this is next to the muscle there is no hindrance to the propagation of the impulse, but at the make the impulse started at the kathode is blocked by the extreme lowering of conductivity at the anode. When the current is descending the kathode is near the muscle, and so the impulse at make reaches the muscle without hindrance; but at the break, the impulse started at the anode has to traverse a region of nerve, the conductivity of which is so lessened that the excitation is not propagated to the muscle.

G. N. Stewart has stated in opposition to the foregoing statements that at the make conductivity is most lowered at the kathode, and at the break at the anode. In other words, conductivity and excitability vary in opposite directions. His results have, however, not been accepted by other physiologists, and are due to a complex set of excitatory and polarisation changes produced by the galvanometric methods he adopted. Gotch's much more trustworthy experiments with the electrometer are directly opposed to those of Stewart. The following simple experiment devised by Gotch appears to be quite conclusive that conductivity like excitability is lessened at the anode when the current is made. Three non-polarisable electrodes are employed (fig. 201), the current is first closed from A_2 to K, and the time which intervenes before the muscle contracts is measured; it is then closed from A_1 to K, and the time again measured. In both cases, excitation occurs at K, but the time of response in the second case (A_1 to K) is longer, because in that case the nerve impulse has to traverse a region of nerve at A_1 in which the power of conduction is lessened.

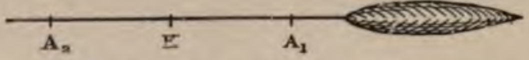

Fig. 201.—Diagram to illustrate Gotch's experiment with triple electrodes.

Sometimes (when the preparation is specially irritable) instead of a simple contraction a tetanus occurs at the make or break of the constant current. This is due to chemical (electrolytic) changes produced by the current, and is liable to occur at the break of a strong ascending current which has been passing for some time into the preparation, or at the make of a strong descending current; both being conditions which increase the excitability of the piece of nerve nearest to the muscle; this is called **Ritter's tetanus**, and may be stopped in the first case by throwing in the current in the same direction, or in the second case by throwing in a current in the opposite direction, *i.e.*, by conditions which lessen the irritability of this piece of nerve.

The same general laws hold for muscle as well as for nerve, but are more difficult to demonstrate; the main fact, however, that the kathode is the stimulating electrode at the make, and the anode at the break, may be shown by the following experiment: if a curarised, that is, a physiologically nerveless muscle, is arranged, as in the experiment, for demonstrating the muscle-wave (see fig. 149, p. 119), and a non-polarisable electrode placed at each end, the muscle-wave at the make of a constant current starts at the kathode and at the break at the anode.

An induced current in the secondary circuit of an inductorium may be regarded as a current of such short duration that the opening and closing are fused in their effects. This is true for all induction currents, whether produced by the make or break of the primary circuit. The kathode will always be the more effective in causing contraction.

RESPONSE OF HUMAN MUSCLES AND NERVES TO ELECTRICAL STIMULATION.

Perhaps the most important outcome of this study of the response of muscle and nerve to electrical stimulation is its application to the muscles and nerves of the human body, because here it forms a most valuable method of diagnosis in cases of disease.

In the normal state, nerves can be stimulated either by induction shocks, or by the make and break of a constant current. In the case of the motor nerves this is shown by the contraction of the muscles they supply; and in the case of the sensory nerves by the sensations that are produced. In the case of the sensory nerves, the sensation produced by the constant current is most intense at the instant of make and break, or when the strength of the current is changed in the direction either of diminution or increase; but there is a slight sensation due doubtless to the electrotonic alterations in excitability which we have been studying, during the whole time that the current is passing.

When the nutrition of the nerves is impaired, much stronger currents of both the induced and constant kinds are necessary to evoke muscular contractions than in the normal state. When the nerves are completely *degenerated* (as, for instance, when they are cut off from the spinal cord, or when the cells in the cord from which they originate are themselves degenerated, as in infantile paralysis) no muscular contraction can be obtained on stimulating the nerves even with the strongest currents.

The changes in the excitability of the muscles are less simple, because in them there are two excitable structures, the terminations of the nerves, and the muscular fibres themselves. Of these, the nerve-fibres are the more sensitive to induction currents, and the faradic stimulation of a muscle under normal circumstances is by means of these motor nerve-endings. Thus we find that its excitability corresponds in degree to that of the motor nerve supplying it. The muscular fibres are, even in the normal state, less sensitive to faradism (that is, a succession of induction shocks) than the nerve, because they are incapable of ready response to stimuli so very short in duration as are the shocks of which a faradic current consists. The proof of this consists in the fact that under the influence of curare, which renders the muscle practically nerveless, the muscle requires a much stronger faradic current to stimulate it than in the normal state. When the nerve is degenerated, the make or break of the constant current stimulates the muscle as readily as in the normal state; but the contraction is propagated more slowly than that which occurs when the nerve-fibres are intact, and is due to the stimulation of the muscular fibres themselves. The fact that, under normal circumstances, the contraction which is caused by the constant current is as quick as that produced by an induction shock, is ground for believing that in health the constant, like the induced current, causes the muscle to contract chiefly by exciting the motor nerves within it.

When the motor nerve is degenerated, and will not respond to any form of electrical stimulation, the muscle also loses all its power of response to induction shocks. The nerve-degeneration is accompanied by changes in the nutrition of the muscular fibres, as is evidenced by their rapid wasting, and any power of response to faradism they possessed in the normal state is lost. But the response to the constant current remains, and is indeed more ready than in health, doubtless in consequence of nutritive changes which develop what the older pathologists called, truly enough, "irritable weakness." There is, moreover, a qualitative as well as a quantitative change. In health the first contraction to occur on gradually increasing the strength of the current is at the negative pole, when the circuit is closed (see Pflüger's law), and a stronger current is required before closure-contraction occurs at the positive pole. But in the morbid state we are discussing, closure-contraction may occur at the positive pole as readily as at the negative pole. This condition is called the "*Reaction of Degeneration.*"

Suppose a patient comes before one with muscular paralysis. This may be due to disease of the nerves, of the cells of the spinal cord, or of the brain. If the paralysis is due to brain disease, the muscles will be slightly wasted owing to disuse, but the electrical irritability of the muscles and nerves will be normal, as they are still in connection with the nerve-cells of the spinal cord that control their nutrition. But if the paralysis is due to disease either of the spinal cord or of the nerves, this nutritive influence can no longer be exercised over the nerves or muscles. The nerves will degenerate; the muscles waste rapidly; the irritability of the nerves to both forms of electrical stimulation will be lost; the muscles will not respond to the faradic current, but in relation to the constant current they will exhibit what we have called the "reaction of degeneration."

This illustrates the value of the electrical method as a means of diagnosis, that is, of finding out what is the matter with a patient. It is also a valuable means of treatment; by making the muscles contract artificially, their nutrition is kept up until restoration of the nerves or nerve-centres is brought about. Another illustration will indicate that the facts regarding electrotonic variation of excitability are true for sensory as well as for motor nerves; in a case of neuralgia, relief will often be obtained by passing a constant current through the nerve; but the pole applied to the nerve must be the anode which produces diminution of excitability, not the kathode which produces the reverse.

Waller has pointed out that Pflüger's law of contraction, as formulated for frogs' muscles and nerves, is true for human muscles and nerves in the main, but there are certain discrepancies. These arise from the method necessarily employed in man being different from those used with a muscle-nerve preparation. In a muscle-nerve preparation the nerve is dissected out, the two electrodes placed on it, and the current has of necessity to traverse the piece of nerve between the two electrodes. In man, the current is applied by means of electrodes or rheophores which consist of metal discs covered with wash leather, and soaked in brine. One of these is placed on the moistened skin over the nerve, and the other on some indifferent point, such as the back. The current finds its way from one electrode to the other, not necessarily through the nerves to any great extent (though it will be concentrated at the nerve as it leaves the anode or reaches the kathode), but diffuses widely through the body, seeking the paths of least resistance. Thus it is impossible to get pure anodic or kathodic effects. If the anode is applied over the nerve, the current enters by a series of points (polar zone), and leaves by a second series of points (peripolar zone). The second series of points is very close to the first, as the current leaves the nerve as soon as possible, seeking less resistant paths. The polar zone will be in the condition of anelectrotonus, the peripolar in that of katelectrotonus, so that although the former effect will predominate, the points being more concentrated, the latter effect may prevent a pure anelectrotonic effect being observed (fig. 202).

Pflüger's law of contraction according to which excitation occurs at the kathode on the make of a constant current, and at the anode on the break, holds good for all excitable tissues. The excitation at the break is probably really due to the make of a polarisation current having its kathode at the former anode, and is therefore fundamentally of the same nature as the make contraction ; or, in general terms, excitation occurs only at the place where a current leaves the excitable tissue. No doubt the effect is determined by the electrolytic changes occurring at the point of entry and exit of the current ; the development of kat-ions must therefore be the chemical change that results in excitation. It is difficult to imagine that in a degenerated muscle there should be a reversal of such a fundamental law, and that excitation should be associated with the development of an-ions. Yet this is supposed to occur in the qualitative change known as the "reaction of degeneration." Page May has investigated this question afresh, and finds that the reversal of the law is only apparent, not real, and is due to the imperfect method which clinical observers must necessarily employ when testing the electrical reaction of muscles through the skin. By the use of appropriate electrodes on the degenerated muscles of animals, it is possible to detect the source of error. Let us substitute a muscle for a nerve in the diagrams of fig. 202 ; the current enters a few fibres at the anode, then spreads in all directions, and leaves the muscle by a number of diffused kathodic points. If the muscle is degenerated, its excitability is high, and the ready response at the anode when the current is made does not really occur at the actual anode, but in the neighbouring and more widespread peripolar kathodes. In other words, degenerated muscle obeys the general law of excitable tissues, and excitation occurs only at the situation where the current leaves the muscle. At the actual anode there is relaxation or absence of effect ; this is obviously not observable through the human skin because the change is very limited in extent ; it can be actually seen in the exposed muscles of an animal.

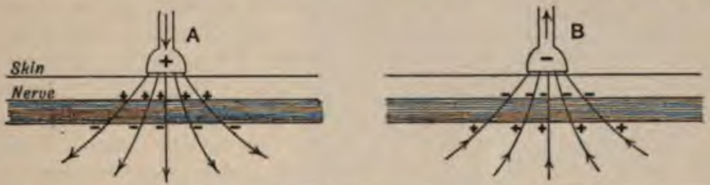

FIG. 202.—Electrodes applied to the skin over a nerve-trunk. In A the polar area is anelectrotonic, and the peripolar katelectrotonic. The former condition, therefore, preponderates, since the current is more concentrated. In B the conditions are reversed, the polar zone corresponding here to the kathode. (After Waller.)

CHAPTER XVII

NERVE-CENTRES

THE nerve-centres consist of the brain and spinal cord; they are characterised by containing nerve-cells, from which the nerve-fibres of the nerves originate. Small collections of nerve-cells are found also in portions of the peripheral nervous system, where they are called *ganglia*. The spinal ganglia on the posterior roots of the spinal nerves, and the sympathetic ganglia are instances of these.

The general arrangement of the cerebro-spinal axis is given in the accompanying diagram. The nerves which take origin from the brain are called cranial nerves; there are twelve pairs of these; some of them, like the olfactory, optic, and auditory nerves, are nerves of special sense; others supply the region of the head with motor and sensory fibres. One pair (the tenth), called the pneumogastric or vagus nerves, are mainly distributed to the viscera of the thorax and abdomen, and a part of another pair (the eleventh), called the spinal accessory nerves, unites with the vagus prior to such distribution. We shall in our subsequent study of the heart, lungs, stomach and other organs have frequently to allude to these nerves. The first two pairs of cranial nerves (the olfactory and the optic) arise from the cerebrum. The remaining ten pairs are connected with the district of grey matter called the floor of the fourth ventricle or its immediate neighbourhood; this tract of grey matter is situated at the lower part of the brain where it joins the spinal cord; this portion of the brain is called the *Bulb* or *Medulla oblongata*.

The spinal nerves are arranged in pairs, 31 in number. Their general structure and functions we have already studied (pp. 168-170).

The more intimate structure of the brain and spinal cord we shall consider at length in subsequent chapters. For the present we shall deal with some of the general aspects of the nerve-centres, both as regards structure and function.

The brain and spinal cord consist of two kinds of tissue, easily distinguishable by the naked eye. They are called respectively *white matter* and *grey matter*.

White matter is composed of medullated nerve-fibres, which differ in structure from the medullated fibres of nerve by having no primitive sheath (neurilemma).

Grey matter is the true central material so far as regards function; that is to say, it is the part which receives and sends out nervous impulses; it is characterised by containing the bodies of the nerve-cells.

In the brain the grey matter is chiefly situated on the surface, forming what is called the *cortex;* the white matter and certain subsidiary masses of grey matter are in the interior.

In the spinal cord, the grey matter is in the interior, the white matter outside.

In both grey and white matter the nerve-cells and nerve-fibres are supported by a peculiar tissue which is called *neuroglia.* It is composed of cells and fibres, the latter being prolonged from the cells. Some of the fibres are radially arranged. They start from the outer ends of the ciliated epithelium cells that line the central canal of the spinal cord and the ventricles of the brain, and diverge constantly branching towards the surface of the organ, where they end by slight enlargements attached to

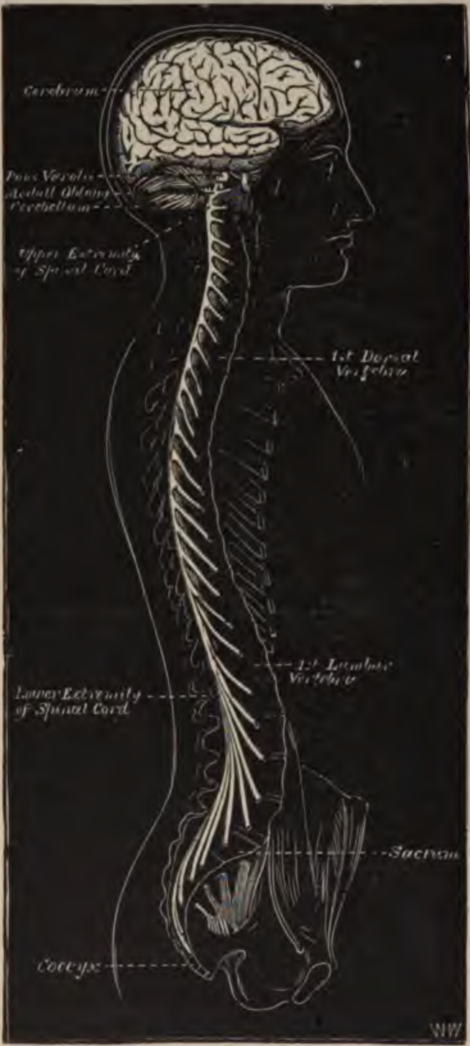

FIG. 203.—View of the cerebro-spinal axis of the nervous system. The right half of the cranium and trunk of the body has been removed by a vertical section; the membranes of the brain and spinal cord have also been removed, and the roots and first part of the fifth and ninth cranial, and of all the spinal nerves of the right side, have been dissected out and laid separately on the wall of the skull and on the several vertebræ opposite to the place of their natural exit from the cranio-spinal cavity. (After Bourgery.)

the pia mater. The other fibres of the tissue are cell processes of the neuroglia or glia cells proper, or spider cells as they are sometimes termed (see fig. 204).

Neuroglia is thus a connective tissue in function, but it is not one in origin. Like the rest of the nervous system, it originates from the outermost layer of the embryo, the epiblast. All true connective tissues are mesoblastic.

Chemically, it is very different from connective tissues. It consists of an insoluble material called *neuro-keratin*, or nerve-horn, similar to the horny substance, keratin, which is found in the surface layers of the epidermis.

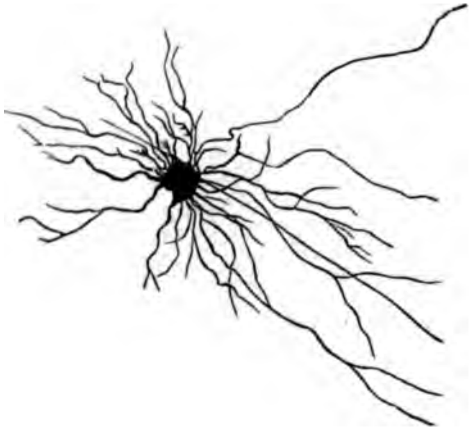

FIG. 204.—Branched neuroglia-cell. (After Stöhr.)

Structure of Nerve-Cells.

Nerve-cells differ a good deal both in shape and size.

In the early embryonic condition, the future nerve-cell is a small nucleated mass of protoplasm without processes. As development progresses branches grow, and by this means it is brought into contact with the branches of other nerve-cells. When the nerve-cells degenerate, as they do in some cases of brain and cord disease, there is a reversal of this process; just as in a dying tree the terminal branches, those most distant from the seat of nutrition, are the first to wither, so it is in the degenerating nerve-cell. If one traces the structure of nerve-cells throughout the zoological series, there is also seen an increase in their complexity, and the number of points of contact produced by an increase in the number and complexity of the branches multiplies (fig. 205).

The simplest nerve-cells known are termed *bipolar*. In the lower animals the two processes come off from the opposite ends of the cells; the cell, in other words, appears as a nucleated enlargement on the course of a nerve-fibre. Fig. 206 (A) shows one of these nerve-cells from the Gasserian ganglion of the pike. The cells of the Gasserian and spinal ganglia in the mammalian embryo are also bipolar, but as development progresses, the two branches become fused for a considerable distance, so that in the fully formed animal each cell appears to be *unipolar*. This is shown in a more diagrammatic way in fig. 187, p. 168. The bifurcation of the nerve-fibre is spoken of as a T-shaped junction. As will be seen in fig. 206 (C), the nerve process has a convoluted course on the surface of the cell before it bifurcates. In these ganglia it should be also noted that each cell is enclosed within a connective tissue sheath, and the nuclei seen are those of the connective tissue corpuscles.

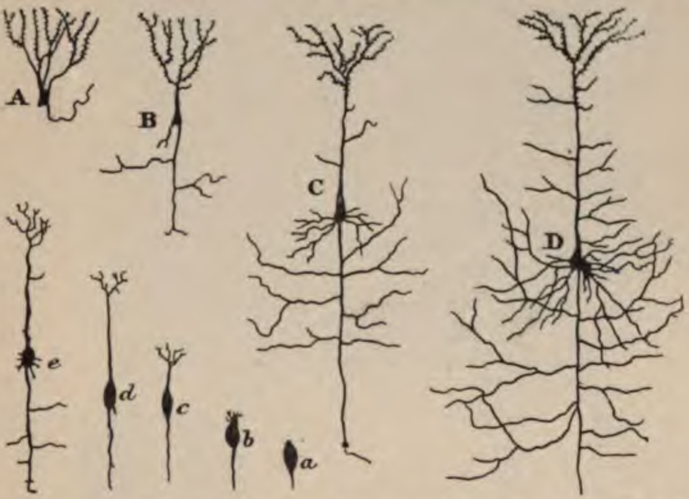

FIG. 205.—Diagram after Ramon y Cajal to show the ontogenetic (or embryological) and phylogenetic (*i.e.* in the animal series) development of a neuron. A, cerebral cell of frog; B, newt; C, mouse; D, man. As the place in the zoological series rises, the neuron increases in complexity and in the number of points of contact; this is produced partly by an increase of the dendrons, partly by an increase in the side branches or collaterals of the axon. *a*, *b*, *c*, *d*, *e*, show the early stages in the development of a similar cell in the human embryo; the first branch of the cell to appear (in *a*) is the axon; the dendrons are later outgrowths. The reversal of this process takes place in primary degeneration.

In the sympathetic ganglia, the cells may have a similar structure, and here also the nucleated sheath is seen. In some cases, however, when there appear to be two fibres connected to a cell, one of them is really derived from another cell, and is passing to end in a ramification which envelopes the ganglion cell; it may sometimes be coiled spirally around the issuing nerve-fibre.

The majority of nerve-cells found in the body are *multipolar*. Here the cell becomes angular or stellate. Fig. 207 shows the usual form of cell present in sympathetic ganglia. From the angles of the cell, branches originate; the majority of these branches divide and subdivide until each ends in an arborescence of fine twigs or fibrils; but one process, and one process only, of each cell becomes the axis cylinder of a nerve-fibre.

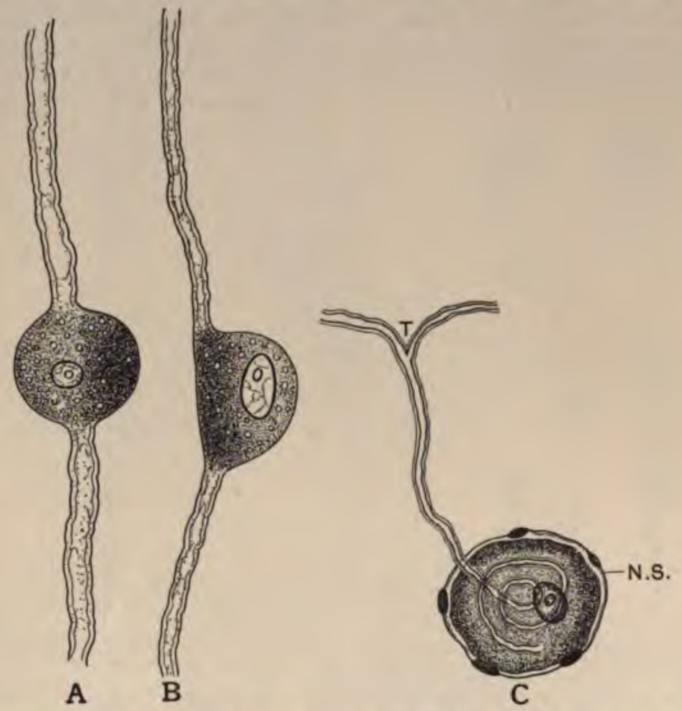

FIG. 206.—Bipolar nerve-cells. A. From the Gasserian ganglion of the pike (after Bidder). B. From a spinal ganglion of a 4½ weeks' human embryo (after His). C. Adult condition of the mammalian spinal ganglion cell: N. S. nucleated sheath; only the nuclei seen in profile are represented. T. is the T-shaped junction (after Retzius).

Passing next to the central nervous system, we here again find the multipolar cell is the principal kind present.

The next figure (fig. 208) shows one of the typical multipolar cells of the spinal cord. Here again, only one process (a) becomes the axis cylinder of a nerve-fibre, and the others break up into arborisations of fibrils. The cells have a finely fibrillar structure, and the fibrils can be traced into the axis cylinder process and the other branches of the cell. Between the fibrils the protoplasm of the cell contains a number of angular or spindle-shaped masses, which have a great affinity of basic aniline dyes like methylene blue. They are known as *Nissl's granules.* These nerve-cells often contain, especially in the adult, granules of pigment, usually yellow, the nature of which has not been determined.

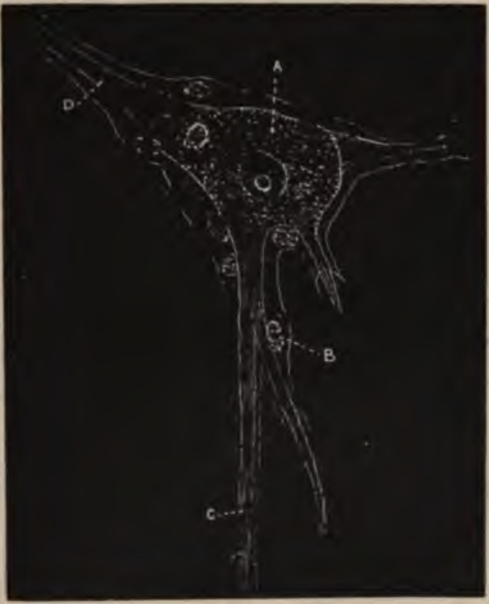

FIG. 207.—An isolated sympathetic ganglion cell of man, showing sheath with nucleated cell lining, B. A. Ganglion cell, with nucleus and nucleolus. C. Branched process. D. Axis cylinder process (Key and Retzius.) × 750.

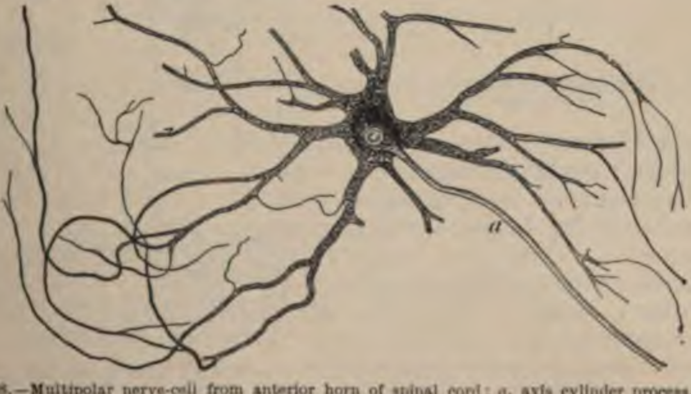

FIG. 208.—Multipolar nerve-cell from anterior horn of spinal cord; *a*, axis cylinder process. (Max Schultze.)

In preparations made by Golgi's chromate of silver method, the cells and their processes are stained an intense black by a deposit of silver. The various structures in the cells (nucleus, granules, fibrils, etc.), are not visible in such preparations, but the great advantage of the method is that it enables one to follow the branches to their finest ramifications. It is thus found that the axis cylinder process is not unbranched, as represented in fig. 208, but invariably gives off side-branches, which are called *collaterals;* these pass into the adjacent nerve-tissue. The axis cylinder then acquires the sheaths, and thus is converted into a nerve-fibre. This nerve-fibre sometimes, as in the nerve-centres after a more or less extended course, breaks up into a terminal arborescence enveloping other nerve-cells; the collaterals also terminate in a similar way. The longest type of axis cylinder is that which passes away from the nerve-centre, and gets bound up with other similarly sheathed axis cylinders to form a nerve; but

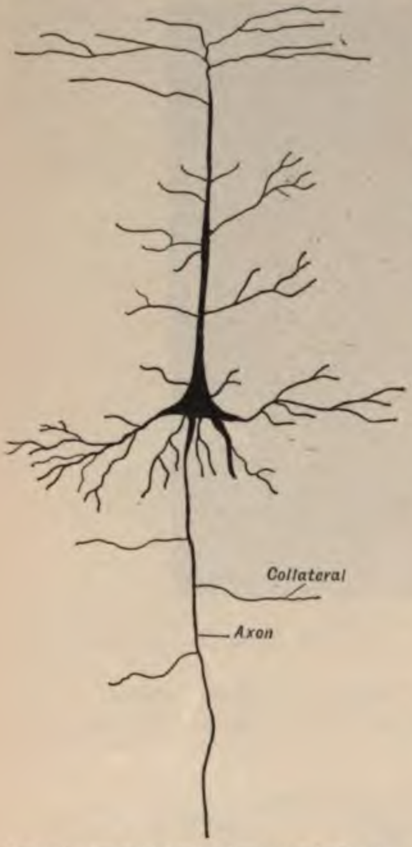

FIG. 209.—Pyramidal cell of human cerebral cortex. Golgi's method.

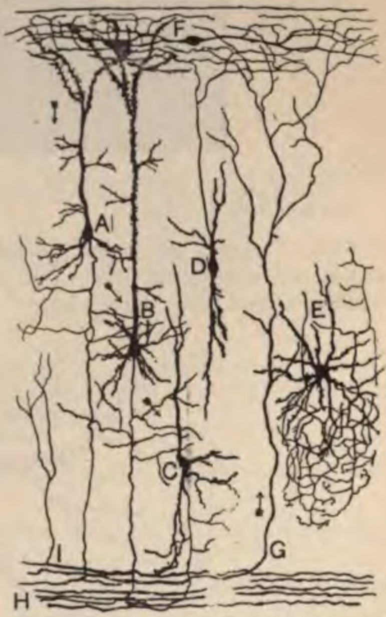

FIG. 210.—Cerebral cortex of mammal, prepared by Golgi's method. A, B, C, D, F, nerve-cells; E, neuroglia-cell. (Ramon y Cajal.)

all ultimately terminate in an arborescence of fibrils in various end organs (end-plates, muscle spindles, etc.).

In the grey matter of the cerebrum the nerve-cells are various in shape and size, but the most characteristic cells are pyramidal in shape. They are especially large and numerous in what are called the motor areas of the brain. The apex of the cell is directed to the surface; the apical process is long and tapering, and finally breaks up into fibrils that lie parallel to the surface of the brain (*tangential fibres*). From the lower angles and other parts branching processes originate; the axis cylinder comes off from the base of the pyramid. (See figs. 209, 210).

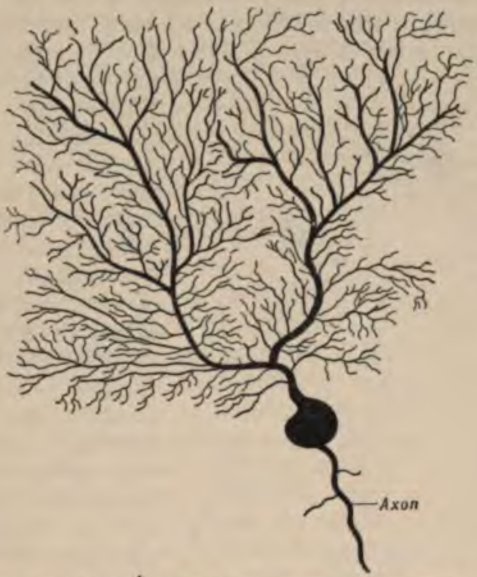

FIG. 211.—Cell of Purkinje from the human cerebellum. Golgi's method. (After Szymonowicz.)

The grey matter of the cerebellum contains a large number of small nerve-cells, and one layer of large cells. These are flask-shaped, and are called the *cells of Purkinje*. The neck of the flask breaks up into branches, and the axis cylinder process comes off from the base of the flask (fig. 211).

The whole nervous system consists of nerve-cells and their branches, supported by neuroglia in the central nervous system, and by connective tissue in the nerves. Some of the processes of a nerve-cell break up almost immediately into smaller branches ending in arborescences of fine twigs; these branches, which used to be called protoplasmic processes, are now termed *dendrons*. One branch becomes the long axis cylinder of a nerve-fibre, but it also ultimately terminates in an arborisation; it is called the *axis cylinder process*, or, more briefly, the *axon*. The term *neuron* or *neurone* is applied to the complete *nerve-unit*, that is, the body of the cell, and all its branches. Some observers have supposed that the axis cylinder process is the only one that conducts nerve impulses, the dendrons being rootlets which suck up nutriment for the nerve-cell. This view has not, however, been accepted; the dendrons may be nutritive, but there is no doubt that they also, like the rest of the nerve-unit, are concerned in the conduction of nerve impulses. A strong piece of evidence in this direction is the fact that the fibrils of the axis cylinder may be traced through the body of the cell into the dendrons.

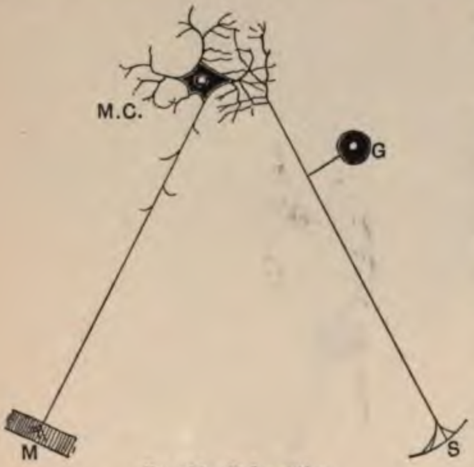

FIG. 212.—Reflex action.

The next idea which it is necessary to grasp is, that each nerve-unit (cell *plus* branches of both kinds) is anatomically independent of every other nerve-unit. There is no true anastomosis of the branches from one nerve-cell with those of another; the arborisations interlace and intermingle, and nerve impulses are transmitted from one nerve-unit to another, through contiguous, but not through continuous structures. A convenient expression for the intermingling of arborisations is *synapse* (literally, a clasping).

Fig. 212 is a diagram of the nervous path in a reflex action. Excitation occurs at S, the skin or other sensory surface, and the impulse is transmitted by the sensory nerve-fibre to the nerve-centre, where it ends not in a cell-body, but by arborising around one or more cell-bodies and their dendrons. The only cell-body in actual continuity with the sensory nerve-fibre is the one in the spinal ganglion (G) from which it grew.

The terminal arborisation of the sensory nerve-fibre merely interlaces with the dendrons of the motor nerve-cell; yet simply by this synapse, the motor nerve-cell (M C) is affected and sends an impulse by its axis cylinder process to the muscle (M).

A very rough illustration which may help one in realising this may be taken as follows: Suppose two trees standing side by side; their stems will represent the axis cylinders; their branches the dendrons. If the trees are close together the branches of one will intermingle with those of the other: there is no actual branch from the one which becomes continuous with any branch of the other; but yet if the stem of one is vigorously shaken, the close intermixture of the branches will affect the other so that it also moves.

Another very important general idea which we must next get hold of, is that a nervous impulse does not necessarily travel along the same nerve-fibre all the way, but there is what we may term a *system of relays.* The nervous system is very often compared to a telegraphic system throughout a country. The telegraph offices represent the nerve-centres, the afferent nerve-fibres correspond to the wires that carry the messages to the central offices, and the efferent nerve-fibres are represented by the wires that convey messages from the central offices to more or less distant parts of the country. This illustration will serve us very well for our present purpose, provided that it is always remembered that a nervous impulse is not electricity. Suppose, now, one wishes to send a message from the metropolis, which will represent the brain, to a distant house, say in the Highlands of Scotland. There is no wire straight from London to that house, but the message ultimately reaches the house; one wire takes the message to Edinburgh; another wire carries it on to the telegraph station in the town nearest to the house in question; and the last part of the journey is accomplished by a messenger on foot or horseback. There are at least two relays on the journey.

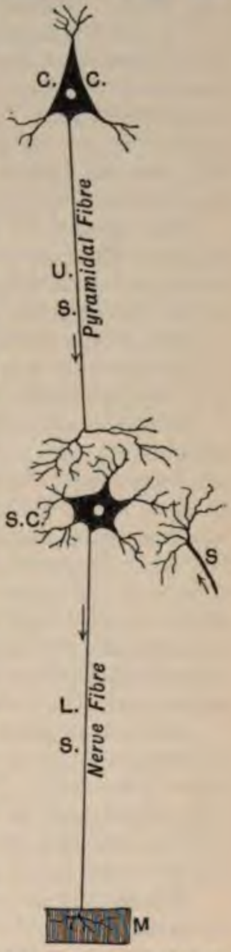

FIG. 213.—Diagram of an element of the motor path. U.S., upper segment; L.S., lower segment; C.C., cell of cerebral cortex; S.C., cell of spinal cord, in anterior cornu; M., the muscle; S., path from sensory nerve-roots. (After Gowers.)

It is just the same with the nervous system. Suppose one wishes to move the arm; the impulse starts in the nerve-cells of the brain, but there are no fibres that go straight from the brain to the muscles of the arm. The impulse travels down the spinal cord, by what are called pyramidal fibres, which form synapses with the nerve-cells of the spinal cord, and from these cells, fresh nerve-fibres pass to the arm-muscles, and continue the impulse. This is shown in the accompanying diagram (fig. 213). The cell of the cerebral grey matter is represented by C. C., the pyramidal nerve-fibre arborises around the cell of the spinal cord (S. C.) from which the motor nerve-fibre arises, and which carries on the impulse. The spinal cord cells are thus surrounded by arborisations (synapses) derived not only from the sensory nerves (S), but by fibres from the upper part of the nervous system. We now see how it is possible that reflex actions in the cord may be controlled by impulses from the brain.

The system of relays is still more complicated in the case of sensory impulses, as we shall see later on; the same is true for the motor path to involuntary muscle, accessory cell-stations being situated in the sympathetic ganglia.

We may now return for a moment to the subject of degeneration. If the nerve-fibre is cut off from its connection with the spinal nerve-cell, the peripheral end degenerates as far as the muscle.

Suppose, now, the pyramidal fibre were cut across, the piece still attached to the brain-cell would remain in a comparatively normal condition, but the peripheral end would degenerate as far as the synapse round the spinal cell (S. C.), but not beyond. We can thus use the degeneration method to trace out tracts of nerve-fibres in the white matter of the central nervous system. The histological change in the fibres is here the same as that already described in the nerves, except that, as there is no primitive sheath, there can be no multiplication of its nuclei; there is instead an over-growth of neuroglia. Degenerated tracts consequently stain differently from healthy white matter, and can be by this means easily traced.

Another method of research which leads to the same results as the degeneration method is called the embryological method. The nerve-fibres which grow from different groups of nerve-cells become fully developed at different dates, and so, by examining brains and cords of embryos of different ages, one is able to make out individual tracts before they have blended in the general mass of white matter.

We shall, however, return to this subject when later on we are studying the physiology of the central nervous system in detail.

The Significance of Nissl's Granules.

If portions of the brain or spinal cord are fixed in absolute alcohol, and sections obtained from the hardened pieces are stained by means of methylene blue, the nerve-cells exhibit a characteristic appearance. The nucleus and nucleolus take up the blue stain, and throughout the cell body a number of angular-shaped masses, which are termed *Nissl's granules*, are also stained blue. These extend some distance into the dendrons, but not into the axon. The substance of which they are composed is termed *chromatoplasm*, or *chromophilic material*. The existence of granules in cells which have an affinity for basic dyes like methylene blue is not at all common; the granules in the majority of the white blood corpuscles, for instance, have an affinity for acid dyes. Micro-chemical methods have shown that the main constituent of the Nissl granules is nucleo-proteid. The name *kinetoplasm* has been given to it by Marinesco in order to express the idea that it forms a source of energy to the cell. It can hardly be denied that the substance of which the granules are composed, forming as it does so large a proportion of the cell-contents, and made of a material in which nuclein forms an important constituent, is intimately related to the nutritional condition of the neuron. Some have even compared it to the granular material, which is present in secreting cells; in these cells before secretion occurs, the granules accumulate, and during the act of secretion they are discharged and converted into constituents of the secretion. It is stated by some observers that the Nissl granules are used up during the discharge of energy from nerve-cells, and it certainly is the case that if the cells are examined after an epileptic fit, in which there has been a very massive discharge of impulses, the Nissl granules have disappeared, or at least broken up into fine dust-like particles, so that the cell presents a more uniform blue staining (see fig. 214). It is, however, doubtful whether this is due to a transformation associated with intense activity, or whether it may not be caused by venosity of the blood. The cells are very sensitive to altered vascular conditions; anæmia, for instance, produces a similar change accompanied with swelling of the cell, and swelling and in extreme cases extrusion of the nucleus. High fever (hyperpyrexia) causes a very similar change, which is doubtless associated with the coagulation of the proteids of the cell-protoplasm by the high temperature.

Since attention has been directed towards the Nissl granules, a literature which has become alarmingly vast during the last few years has sprung up in relation to them. This is quite easy to understand, for neurologists have by this sensitive test been able to identify changes in the cells which could not be detected by the previous methods of staining. Thus the cells have been examined in various diseases, and after being subjected to the action of various poisons. In a new subject of this kind there is, as would be expected, considerable divergence of views, and even the fundamental question has not yet been answered satisfactorily whether the Nissl granules are present as such in the living cell, or whether they are artifacts produced by the fixative action of strong alcohol. The fact that they cannot be demonstrated when the cells are stained by the injection of methylene blue into the circulation before the animal is killed is a very strong piece of evidence in favour of the latter view. But, whichever view is correct, the method is a valuable one, and Nissl's views on this question appear to be indisputable: they are briefly as follows:—Healthy cells fixed and stained in a constant manner will appear the same under constant optical conditions, and the appearances then seen form the equivalent of such healthy cells during life. It follows that if the cells prepared by the same method and examined under the same conditions show a difference from the equivalent or symbol of healthy cells, the difference is the measure of some change that has occurred during life.

Chromatolysis is the term applied to designate the disappearance or disintegration of the Nissl granules. The process generally begins at the periphery of the cell and in the dendrons, but in advanced cases the whole cell may be affected. We have already alluded to the fact that chromatolysis occurs in various abnormal states, and the diminution of the chromophilic nucleo-proteid indicates a diminution of the vital interaction of the highly phosphorised nucleus with the surrounding cell protoplasm. Chromatolysis alone is not indicative of cell destruction, and a cell may recover its function afterwards. The integrity of the nucleus and of the fibrils is much more important to the actual vitality of the cell.

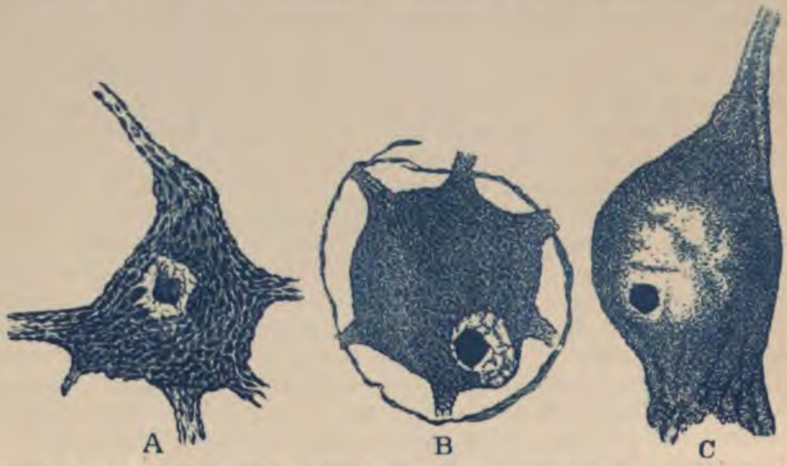

FIG. 214.—Nissl's granules. A. Normal pyramidal cell of human cerebral cortex. B. Swollen œdematous pyramidal cell from a case of status epilepticus. Notice diffuse staining, and absence of Nissl's granules; the nucleus is enlarged and eccentric. The lymph space around the cell is dilated. C. Pyramidal cell of dog after ligature of vessels going to brain and consequent anæmia. Notice great swelling of the nucleus, and advanced chromatolysis, most marked at the periphery of the cell. 700 diameters. (After Mott.)

When a nerve-fibre is cut across, the distal segment undergoes Wallerian degeneration; this is an acute change. But the nerve-cell and the piece of the nerve-fibre still attached to it do not remain unaffected. If regeneration of the fibre, and restoration of function takes place, no change is observable. But if regeneration does not occur (and it never takes place in the central nervous system), the cell and its processes undergo a slow chronic wasting; one of the earliest signs of this *disuse atrophy* is chromatolysis. Warrington has recently stated a still more interesting fact, namely, that section of the posterior roots causes chromatolysis in the anterior horn cells of the same side; this indicates that the loss of sensory stimuli produces a depression of the activity and metabolic functions of the spinal motor cells. We shall see later on that this accords quite well with the physiological effects observed under these conditions.

Classification of Nerve-cells according to their Function.

In addition to the anatomical classification of the nerve-cells already given, Schäfer separates them into four chief classes on a physiological basis:—

1. Afferent or sensory root cells.
2. Efferent root cells.
3. Intermediary cells.
4. Distributing cells.

1. *Afferent root cells.*—Originally such cells are situated at the periphery, and are connected with a process or afferent fibre which passes to and arborises among the nerve-cells of the central nervous system. This primitive condition is well seen in the earthworm, and persists in the olfactory cells of all vertebrates.

As evolution progresses, the peripheral cell sinks below the integument, leaving a process at the surface; this is seen in the worm Nereis (see fig. 215). Ultimately the body of the cell approaches close to the central nervous system, in the spinal ganglion of the posterior root, and the peripheral sensory nerve-fibre is correspondingly longer.

The afferent root cells, such as those of the spinal ganglia and the corresponding ganglia of the cranial nerves, are peculiar in possessing no dendrons.

2. *Efferent root cells.*—The anterior horn cells of the spinal cord are instances of these; their axons go directly to muscle fibres.

3. *Intermediary cells.*—These receive impulses from afferent cells, and transmit them either directly, or indirectly through other intermediary cells to efferent cells. The majority of the cells of the brain and cord come under this heading; they serve the purposes of association and co-ordination, and form the basis of psychical phenomena.

4. *Distributing cells.*—These are the cells of the sympathetic

ganglia; they are situated outside the central nervous system; they receive impulses from efferent cells in the central nervous system, and distribute them to involuntary muscles and secreting glands.

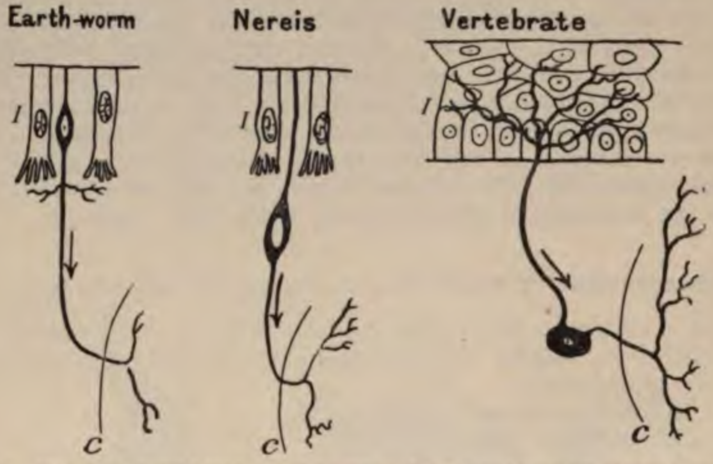

FIG. 215.—Diagram to illustrate the primitive conditions of the afferent nerve-cell, and the manner in which it becomes altered in the process of evolution. (After Retzius.) I, integument; C, central nervous system; the arrows show the direction in which the impulse passes.

The Law of Axipetal Conduction.

A general law has been laid down by van Gehuchten and Cajal, that all nerve impulses are axipetal, that is, they pass towards the attachment of the axon, by which they leave the body of the cell. In other words, the direction of an impulse is towards the body of the cell in the dendrons, and away from it in the axon. When we further consider that every nervous pathway is formed of a chain of cells, and that the impulse always takes the "forward direction," we see that there is what we may compare to a valved action which permits the passage of impulses in one direction only. The synapses are the situations of these so-called valves.

On the onward propagation of a nerve impulse through a chain of neurons, its passage is delayed at each synapse, hence there is additional "lost time" at each of these blocks. The relative number of the blocks furnishes a key to the differences found in reaction time for different reflexes and psychical processes. This we may illustrate by two examples, one taken from the frog, the other from man.

1. If a frog's posterior root is stimulated, the time lost in the spinal cord when the gastrocnemius of the same side contracts is 0·008 sec.; if the opposite gastrocnemius contracts, the additional

lost time is 0·004 sec. If we assume that in the latter case, two extra synapses have to be jumped, the delay at each is 0·002 sec.

2. In the case of the eye and ear in man the total length of the pathway to the brain is approximately the same, and so the reaction times might be expected to be equal; but this is not the case; the reaction time in response to a sudden sound is 0·150 sec., in response to a sudden flash of light 0·195 sec. The greater delay in response to a visual stimulus directly corresponds to the greater number of synapses through which it has to travel (see later, in the structure of the visual and auditory mechanisms).

The valved condition of nervous paths also explains another difficulty. We have seen in p. 173 that under certain circumstances a nervous impulse will travel in both directions along a nerve. Yet when we stimulate the motor fibres in an anterior spinal root, the only effect is a contraction of muscles; there is no effect propagated backwards in the spinal cord. No doubt a nervous impulse does travel backwards to the anterior horn cells, but it is there extinguished, it cannot jump the synapses backwards, and there is no negative variation to be detected in a galvanometer connected to the pyramidal tracts in the cord.

The law of axipetal conduction is no doubt true for the majority of neurons. But there is at any rate one very striking exception, namely, in the typical afferent root cells; here the impulse passes to the body of the cell by one axon from the periphery, and away from it to the spinal cord by the other. To say, as some do, that the peripheral process is really a dendron because it conducts impulses centrifugally is simply arguing in a circle.

CHAPTER XVIII

THE CIRCULATORY SYSTEM

THE circulatory system consists of the *heart*, the *arteries*, or vessels that carry the blood from the heart to other parts of the body, the *veins*, or vessels that carry the blood back to the heart again, and the *capillaries*, a network of minute tubes which connect the terminations of the smallest arteries to the commencements of the smallest veins. We shall also have to consider in connection with the circulatory system, (1) the *lymphatics*, which are vessels that convey back the lymph (the fluid which exudes through the thin walls of the blood-capillaries) to the large veins near their entrance into the heart, and (2) the large lymph spaces contained in the *serous membranes*.

The Heart.

This is the great central pump of the circulatory system. It lies in the chest between the right and left lungs (fig. 216), and is enclosed in a covering called the *pericardium*. The pericardium is an instance of a serous membrane. Like all serous membranes it consists of two layers; each consists of fibrous tissue containing elastic fibres; one layer envelopes the heart and forms its outer covering or *epicardium;* this is the *visceral* layer of the pericardium; the other layer of the pericardium, called its *parietal* layer, is situated at some little distance from the heart, being attached below to the diaphragm, the partition between the thorax and the abdomen. The visceral and parietal layers are continuous for a short distance along the great vessels at the base of the heart, and so form a closed sac. This sac is lined by endothelium; in health it contains just enough lymph (pericardial fluid) to lubricate the two surfaces and enable them to glide over each other smoothly during the movements of the heart. The presence of elastic fibres in the epicardium enables it to follow without hindrance the changing shape of the heart itself; but the parietal layer of the pericardium appears to be inextensible, and so it limits the dilatation of the heart.

The pericardium is a comparatively simple serous membrane, because the organ it encloses is a single one of simple external form. All serous membranes are of similar structure; thus the *pleura* which encloses the lung, and the *peritoneum* which encloses the abdominal viscera differ from it only in anatomical arrangement. The great complexity of the peritoneum is due to its enclosing so many organs. Every serous membrane consists of a visceral layer applied to the organ or organs it encloses; and a parietal layer continuous with this in contiguity with the parietes or body-walls.

The Chambers of the Heart.—The interior of the heart is divided by a longitudinal partition into two chief cavities—right and left. Each of these chambers is again subdivided transversely into an upper and a lower portion, called respectively, auricle and ventricle, which freely communicate one with the other; the aperture of communication, however, is guarded by valves, so disposed as to allow blood to pass freely from the auricle into the ventricle, but not in the opposite direction. There are thus four cavities in the heart—the auricle and ventricle of one side being quite separate from those of the other (figs. 217, 218).

The right auricle is situated at the right part of the base of the heart in front. It is a thin walled cavity of quadrilateral shape, prolonged at one corner into a tongue-shaped portion, the right auricular *appendix*, which slightly overlaps the exit of the aorta, from the heart.

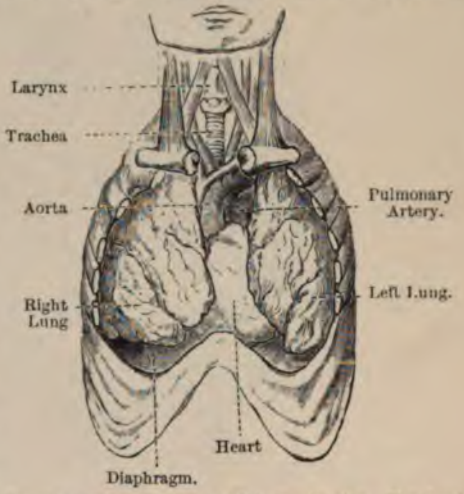

FIG. 216.—View of heart and lungs *in situ*. The front portion of the chest-wall and the outer or *parietal* layers of the pleuræ and pericardium have been removed. The lungs are partly collapsed.

The interior is smooth, being lined with the general lining of the heart, the *endocardium*, and into it open the superior and inferior venæ cavæ, or great veins, which convey the blood from all parts of the body to the heart. The opening of the inferior cava is protected and partly covered by a membrane called the *Eustachian valve*. In the posterior wall of the auricle is a slight depression called the *fossa ovalis*, which corresponds to an opening between the right and left auricles which exists in fœtal life. The coronary *sinus*, or the dilated portion of the left coronary vein, also opens into this chamber.

The right ventricle occupies the chief part of the anterior surface of the heart, as well as a small part of the posterior surface; it forms the right margin of the heart. It takes no part in the formation of the apex. On section its cavity, in consequence of the encroachment upon it of the septum ventriculorum, is crescentic (fig. 219); into it are two openings, the auriculo-ventricular at the base and the opening of the pulmonary artery also at the base, but more to the left; both orifices are guarded by valves, the former called *tricuspid* and the latter *semilunar*. In this ventricle are also the projections of the muscular tissue called *columnæ carneæ* (described at length, p. 212).

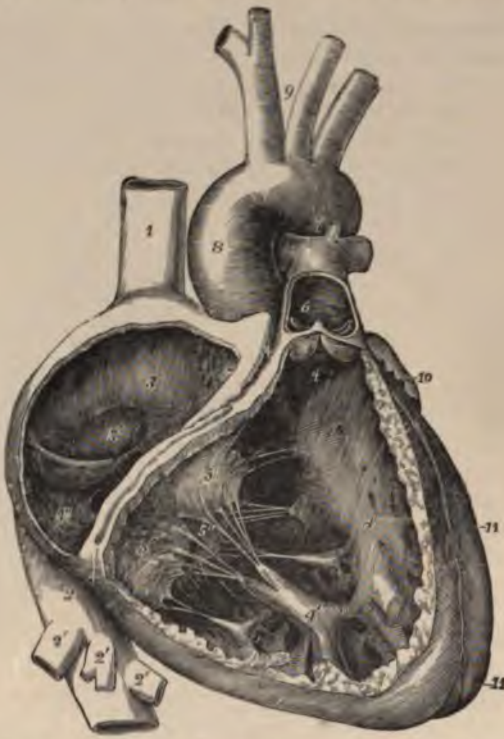

FIG. 217.—The right auricle and ventricle opened, and a part of their right and anterior walls removed, so as to show their interior. $\frac{1}{2}$.—1, superior vena cava; 2, inferior vena cava; 2', hepatic veins cut short; 3, right auricle; 3', placed in the fossa ovalis, below which is the Eustachian valve; 3'', is placed close to the aperture of the coronary vein; + +, placed in the auriculo-ventricular groove, where a narrow portion of the adjacent walls of the auricle and ventricle has been preserved; 4, 4, cavity of the right ventricle, the upper figure is immediately below the semilunar valves; 4', large columna carnea or musculus papillaris; 5, 5', 5'', tricuspid valve; 6, placed in the interior of the pulmonary artery, a part of the anterior wall of that vessel having been removed, and a narrow portion of it preserved at its commencement, where the semilunar valves are attached; 7, concavity of the aortic arch close to the cord of the ductus arteriosus; 8, ascending part or sinus of the arch covered at its commencement by the auricular appendix and pulmonary artery; 9, placed between the innominate and left carotid arteries; 10, appendix of the left auricle; 11, 11, the outside of the left ventricle, the lower figure near the apex. (Allen Thomson.)

The left auricle is situated at the left and posterior part of the base of the heart, and is best seen from behind. It is quadrilateral, and receives on either side two pulmonary veins. The auricular appendix is the only part of the auricle seen from the front, and corresponds with that on the right side, but is thicker, and the interior is smoother. The left auricle is only slightly thicker than the right. The left auriculo-ventricular orifice is oval, and a little

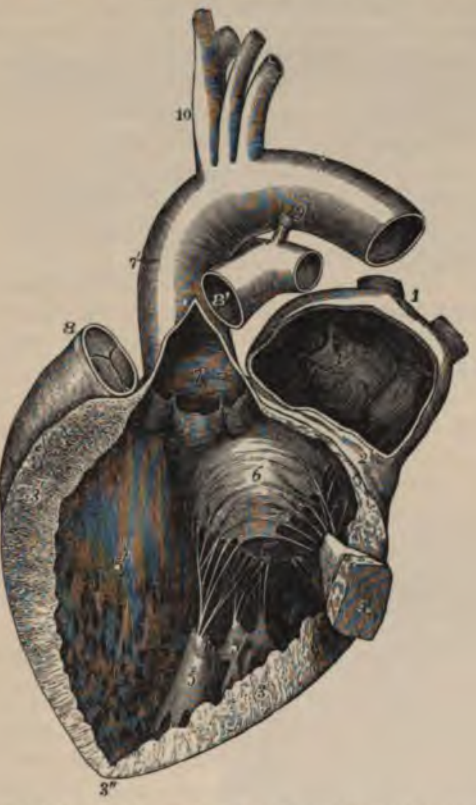

FIG. 218.—The left auricle and ventricle opened and a part of their anterior and left walls removed. ½. —The pulmonary artery has been divided at its commencement; the opening into the left ventricle is carried a short distance into the aorta between two of the segments of the semilunar valves; and the left part of the auricle with its appendix has been removed. The right auricle is out of view. 1, the two right pulmonary veins cut short; their openings are seen within the auricle; 1′, placed within the cavity of the auricle on the left side of the septum and on the part which forms the remains of the valve of the foramen ovale, of which the crescentic fold is seen towards the left hand of 1′; 2, a narrow portion of the wall of the auricle and ventricle preserved round the auriculo-ventricular orifice; 3, 3′, the cut surface of the walls of the ventricle, seen to become very much thinner towards 3″, at the apex; 4, a small part of the anterior wall of the left ventricle which has been preserved with the principal anterior columna carnea or musculus papillaris attached to it; 5, 5, musculi papillares; 5′, the left side of the septum, between the two ventricles, within the cavity of the left ventricle; 6, 6′, the mitral valve; 7, placed in the interior of the aorta, near its commencement and above the three segments of its semilunar valve which are hanging loosely together; 7′, the exterior of the great aortic sinus; 8, the root of the pulmonary artery and its semilunar valves; 8′, the separated portion of the pulmonary artery remaining attached to the aorta by 9, the cord of the ductus arteriosus; 10, the arteries rising from the summit of the aortic arch. (Allen Thomson.)

smaller than that on the right side. There is a depression on the septum between the auricles, which is a vestige of the foramen between them, that exists in fœtal life.

The left ventricle occupies the chief part of the posterior surface. In it are two openings very close together, viz., the auriculo-ventricular and the aortic, guarded by the valves corresponding to those of the right side of the heart, viz., the *bicuspid* or *mitral* and the *semilunar*. The first opening is at the left and back part of the base of the ventricle, and the aortic in front and towards the right. In this ventricle, as in the right, are the columnæ carneæ, which are smaller but more closely reticulated. They are chiefly found near the apex and along the posterior wall. The walls of the left ventricle, which are nearly half an inch in thickness, are, with the exception of the apex, about three times as thick as those of the right.

Capacity of the Chambers.—During life each ventricle is capable of containing about three ounces of blood. The capacity of the auricles is rather less than that of the ventricles: the thickness of their walls is considerably less. The latter condition is adapted to the small amount of force which the auricles require in order to empty themselves into their adjoining ventricles; the former to the circumstance of the ventricles being partly filled with blood before the auricles contract.

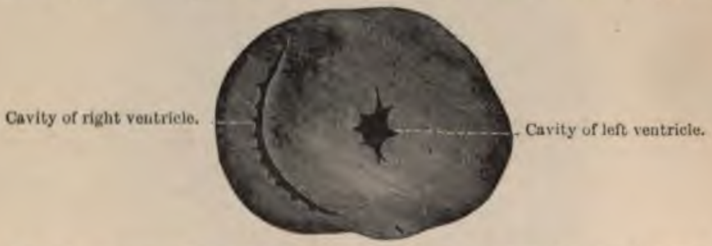

FIG. 219.—Transverse section of bullock's heart in a state of cadaveric rigidity. (Dalton.)

Size and Weight of the Heart.—The heart is about 5 inches long (about 12·6 cm.), 3⅛ inches (8 cm.) greatest width, and 2½ inches (6·3 cm.) in its extreme thickness. The average weight of the heart in the adult is from 9 to 10 ounces (about 300 grms.); its weight gradually increases throughout life till middle age; it diminishes in old age.

Structure.—The walls of the heart are constructed almost entirely of layers of muscular fibres (figs. 113 and 220); but a ring of connective tissue, to which some of the muscular fibres are attached, is inserted between each auricle and ventricle, and forms the boundary of the *auriculo-ventricular* opening. Fibrous tissue also exists at the origins of the pulmonary artery and aorta.

The muscular fibres of each auricle are in part continuous with those of the other, and partly separate; and the same remark holds true for the ventricles. Some muscular fibres also pass across the tendinous ring which separates each auricle from the corresponding ventricle.

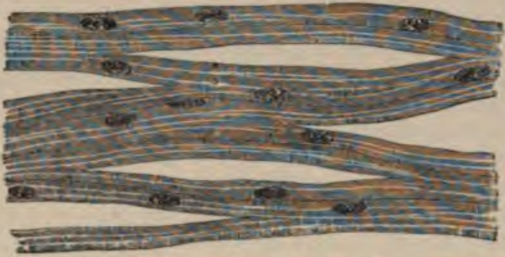

FIG. 220.—Network of muscular fibres from the heart of a pig. The nuclei are well shown. × 450. (Klein and Noble Smith.)

Endocardium.—As the heart is clothed on the outside by the epicardium, so its cavities are lined by a smooth membrane, the *endocardium*, which is directly continuous with the internal lining of the arteries and veins. The endocardium is composed of connective tissue with a large admixture of elastic fibres; its inner surface is covered by endothelium. Here and there muscular fibres are sometimes found in the tissue of the endocardium.

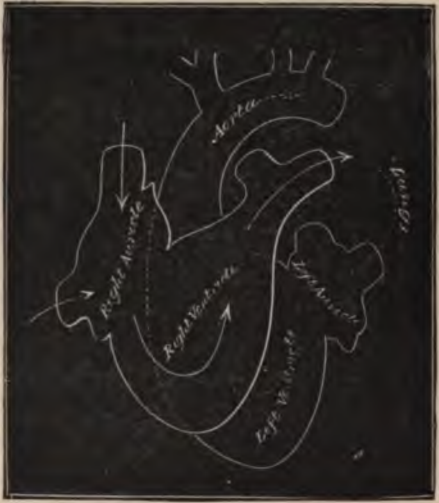

FIG. 221.—Diagram of the circulation through the heart. (Dalton.)

Valves.—The arrangement of the heart's valves is such that the blood can pass only in one direction (fig. 221).

The *tricuspid* valve (5, fig. 217) presents *three* principal cusps or subdivisions, and the mitral or *bicuspid* valve has *two* such portions (6, fig. 218). But in both valves there is between each two principal portions a smaller one: so that more properly, the tricuspid may be described as consisting of six, and the mitral of four, portions. Each portion is of triangular form. Its base is continuous with the bases of the neighbouring portions, so as to form an annular membrane around the auriculo-ventricular opening, and is fixed to a tendinous ring which encircles the orifice between the auricle and ventricle, and receives the insertions of the muscular fibres of both. In each principal cusp may be distinguished a central part, extending from base to apex, and including about half its width. It is thicker and much tougher than the border pieces or edges.

While the bases of the cusps of the valves are fixed to the tendinous rings, their ventricular surface and borders are fastened by slender tendinous fibres, the *chordæ tendineæ,* to the internal surface of the walls of the ventricles, the muscular fibres of which project into the ventricular cavity in the form of bundles or columns—the *columnæ carneæ.* These columns are not all alike, for while some are attached along their whole length on one side, and by their extremities, others are attached only by their extremities; and a third set, to which the name *musculi papillares* has been given, are attached to the wall of the ventricle by one extremity only, the other projecting, papilla-like, into the cavity of the ventricle (5, fig. 218), and having attached to it chordæ tendineæ. Of the tendinous cords, besides those which pass to the margins of the valves, there are some of especial strength, which pass to the edges of the middle and thicker portions of the cusps before referred to. The ends of these cords are spread out in the substance of the valve, giving its middle piece its peculiar strength and toughness; and from the sides numerous other more slender and branching cords are given off, which are attached all over the ventricular surface of the adjacent border-pieces of the principal portions of the valves, as well as to those smaller portions which have been mentioned as lying one between each two principal ones. Moreover, the musculi papillares are so placed that, from the summit of each, tendinous cords proceed to the adjacent halves of two of the principal divisions, and to one intermediate or smaller division, of the valve.

The preceding description applies equally to the mitral and tricuspid valve; but it should be added that the mitral is considerably thicker and stronger than the tricuspid, in accordance with the greater force which it is called upon to resist.

The *semilunar valves* guard the orifices of the pulmonary artery and of the aorta. They are nearly alike on both sides of the heart; but the aortic valves are altogether thicker and more strongly constructed than the pulmonary valves, in accordance with the greater pressure which they have to withstand. Each valve consists of three parts which are of semilunar shape, the convex margin of each being attached to a fibrous ring at the place of junction of the artery to the ventricle, and the concave or nearly straight border being free, so as to form a little pouch like a watch-pocket (7, fig. 218). In the centre of the free edge of the pouch, which contains a fine cord of fibrous tissue, is a small fibrous nodule, the *corpus Arantii,* and from this and from the attached border fine fibres extend into every part of the mid substance of the valve, except a small lunated space just within the free edge, on each side of the corpus Arantii. Here the valve is thinnest, and composed of little more than the endocardium. Thus constructed and attached, the three semilunar pouches are placed side by side around the arterial orifice of each ventricle; they are separated by the blood passing out of the ventricle, but immediately afterwards are pressed together so as to prevent any return (6, fig. 217, and 7, fig. 218). Opposite each of the semilunar cusps, both in the aorta and pulmonary artery, there is a bulging outwards of the wall of the vessel: these bulgings are called the *sinuses of Valsalva.* The valves of the heart are formed of a layer of closely woven connective and elastic tissue, over which, on every part, the endocardium is reflected.

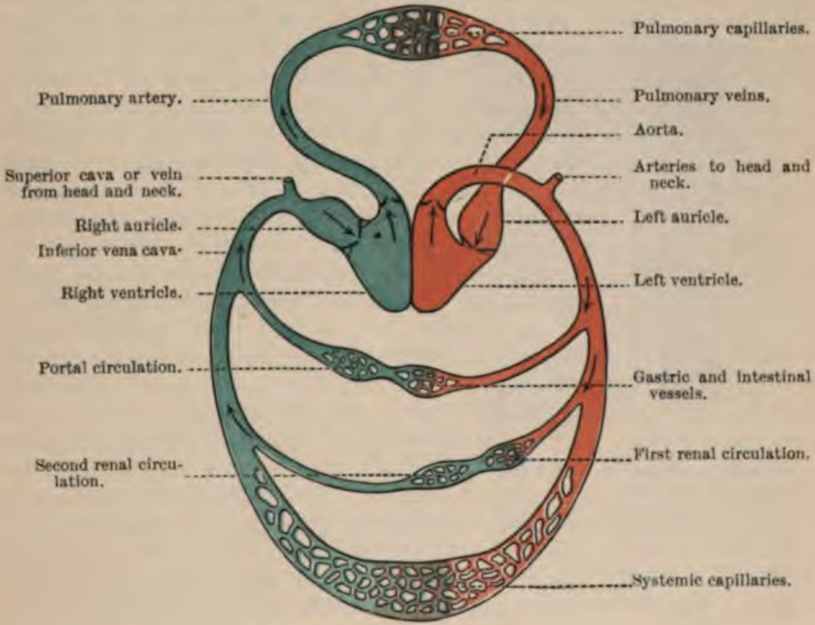

FIG. 222.—Diagram of the circulation.

Course of the Circulation.

The blood is conveyed away from the left ventricle (as in the diagram, fig. 222) by the aorta to the *arteries,* and returned to the right auricle by the *veins*, the arteries and veins being continuous with each other at the far end by means of the *capillaries.*

From the right auricle the blood passes to the right ventricle, then by the pulmonary artery, which divides into two, one for each lung, then through the pulmonary capillaries, and through the pulmonary veins (two from each lung) to the left auricle. From here it passes into the left ventricle, which brings us back to where we started from.

The complete circulation is thus made up of two circuits, the one, a shorter circuit from the right side of the heart to the lungs and back again to the left side of the heart; the other and larger circuit, from the left side of the heart to all parts of the body and back again to the right side. The circulations through the lungs and through the system generally are respectively named the **Pulmonary** and **Systemic** or *lesser* and *greater* circulations. It will be noticed also in the same figure that a portion of the stream of blood having been diverted once into the capillaries of the intestinal canal, and some other abdominal organs, and gathered up again into a single stream, is a second time divided in its passage through the liver, before it finally reaches the heart and completes a revolution. This subordinate stream through the liver is called the **Portal** circulation. A somewhat similar accessory circulation is that through the kidneys, called the **Renal** circulation. The difference of colours in fig. 222 indicates roughly the difference between *arterial* and *venous* blood. The blood is oxygenated in the lungs, and the formation of oxyhæmoglobin gives to the blood a bright red colour. This oxygenated or arterial blood (contained in the pulmonary veins, the left side of the heart, and systemic arteries) is in part reduced in the tissues, and the deoxygenated hæmoglobin is darker in tint than the oxyhæmoglobin; this venous blood passes by the systemic veins to the right side of the heart and pulmonary artery to the lungs, where it once more receives a fresh supply of oxygen.

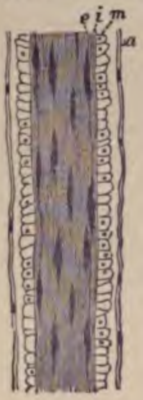

FIG. 223.—Minute artery viewed in longitudinal section. *e.* Nucleated endothelial membrane, with faint nuclei in lumen, looked at from above. *i.* Elastic membrane. *m.* Muscular coat or tunica media. *a.* Tunica adventitia. (Klein and Noble Smith.) × 250.

N.B.—It should, however, be noted that the lungs, like the rest of the body, are also supplied with arterial blood, which reaches them by the bronchial arteries.

The Arteries.

The arterial system begins at the left ventricle in a single large trunk, the aorta, which almost immediately after its origin gives off in the thorax three large branches for the supply of the head, neck, and upper extremities; it then traverses the thorax and abdomen, giving off branches, some large and some small, for the supply of the various organs and tissues it passes on its way. In the abdomen it divides into two chief branches, for the supply of the lower extremities. The arterial branches wherever given off divide and subdivide, until the calibre of each subdivision becomes very minute, and these minute vessels lead into capillaries. Arteries are, as a rule, placed in situations protected from pressure and other dangers, and are, with few exceptions, straight in their course, and frequently communicate (anastomose or inosculate) with other arteries. The branches are usually given off at an acute angle, and the sum of the sectional areas of the branches of an artery generally exceeds that of the parent trunk; and as the distance from the origin is increased, the area of the combined branches is increased also. After death, arteries are usually found dilated (not collapsed as the veins are) and empty, and it was to this fact that their name (ἀρτηρία, the windpipe) was given them, as the ancients believed that they conveyed air to the various parts of the body. As regards the arterial system of the lungs, the pulmonary artery is distributed much as the arteries belonging to the general systemic circulation.

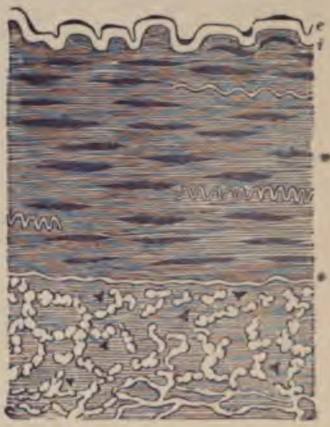

FIG. 224.—Transverse section through a large branch of the inferior mesenteric artery of a pig. *e*, endothelial membrane; *i*, tunica elastica interna, no subendothelial layer is seen; *m*, muscular tunica media, containing only a few wavy elastic fibres; *e*, *e*, tunica elastica externa, dividing the media from the connective-tissue adventitia, *a*. (Klein and Noble Smith.) × 350.

Structure.—The wall of an artery is composed of the following three coats:—

(*a*) The *external coat* or *tunica adventitia* (figs. 223 and 224, *a*), the strongest part of the wall of the artery, is formed of areolar tissue, with which is mingled throughout a network of elastic fibres. At the inner part of this outer coat the elastic network forms, in some arteries, so distinct a layer as to be sometimes called the *external elastic coat* (fig. 224, *e*).

(*b*) The *middle coat* (fig. 224, *m*) is composed of both muscular and elastic fibres, with a certain proportion of areolar tissue. In the larger arteries (fig. 226) its thickness is comparatively as well as absolutely much greater than in the small ones; it constitutes the greater part of the arterial wall. The muscular fibres are unstriped (fig. 225), and are arranged for the most part transversely to the long axis of the artery; while the elastic element, taking also a transverse direction, is disposed in the form of closely interwoven and branching fibres, which intersect in all parts the layers of muscular fibres. In arteries of various sizes there is a difference in the proportion of the muscular and elastic element, elastic tissue preponderating in the largest arteries, and unstriped muscle in those of medium and small size.

(*c*) The *internal coat* is formed by a layer of elastic tissue, called the *fenestrated membrane of Henle.* Its inner surface is lined with a delicate layer of elongated endothelial cells (fig. 224, *e*), which make it smooth, so that the blood may flow with the smallest possible amount of resistance from friction. Immediately external to the endothelial lining of the artery is fine connective tissue (*sub-endothelial layer*) with branched corpuscles. Thus the internal coat consists of three parts, (*a*) an endothelial lining, (*b*) the sub-endothelial layer, and (*c*) elastic layer.

Vasa Vasorum.—The walls of the arteries are, like other parts of the body, supplied with little arteries, ending in capillaries and veins, which, branching throughout the external coat, extend for some distance into the middle, but do not reach the internal coat. These nutrient vessels are called *vasa vasorum.*

Nerves.—Most of the arteries are surrounded by a plexus of sympathetic nerves, which twine around the vessel very much like ivy round a tree. They terminate in a plexus between the muscular fibres (fig. 227).

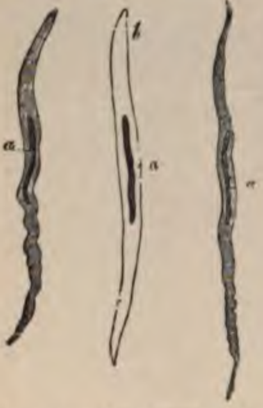

FIG. 225.—Muscular fibre-cells from human arteries, magnified 350 diameters. (Kölliker.) *a.* Nucleus. *b.* A fibre-cell treated with acetic acid.

The Veins.

The venous system begins in small vessels which are slightly larger than the capillaries from which they spring. These vessels are gathered up into larger and larger trunks until they terminate (as regards the systemic circulation) in the two venæ cavæ and the coronary veins, which enter the right auricle, and (as regards the pulmonary circulation) in four pulmonary veins, which enter the left auricle. The total capacity of the veins diminishes as they approach the heart; but, as a rule, their capacity is two or three times that of their corresponding arteries. The pulmonary veins, however, are an exception to this rule, as they do not exceed in capacity the pulmonary arteries. The veins are found after death more or less collapsed, owing to their want of elasticity. They are usually distributed in a superficial and a deep set which communicate frequently in their course.

Structure.—In structure the coats of veins bear a general resemblance to those of arteries (fig. 228). Thus, they possess outer, middle, and internal coats.

(*a*) The *outer* coat is constructed of areolar tissue like that of the arteries, but it is thicker. In some veins it contains muscular fibres, which are arranged longitudinally.

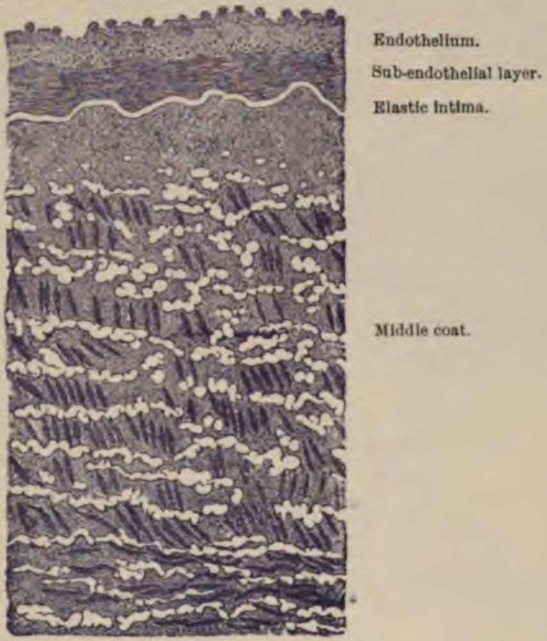

FIG. 226.—Transverse section of aorta through internal and about half the middle coat.

(*b*) The *middle* coat is considerably thinner than that of the arteries; it contains circular unstriped muscular fibres, mingled with a few elastic fibres and a large proportion of white fibrous tissue. In the large veins, near the heart, namely, the *venæ cavæ* and pulmonary veins, the middle coat is replaced, for some distance from the heart, by circularly arranged striped muscular fibres, continuous with those of the auricles. The veins of bones, and of the central nervous system and its membranes have no muscular tissue.

(*c*) The *internal* coat of veins has a very thin fenestrated membrane, which may be absent in the smaller veins. The endothelium is made up of cells elongated in the direction of the vessel, but wider than in the arteries.

Valves.—The chief influence which the veins have in the circulation is effected with the help of the valves, contained in all veins subject to local pressure from the muscles between or near which they run. The general construction of these valves is similar to that of the semilunar valves of the aorta and pulmonary artery, already described; but their free margins are turned in the opposite direction, *i.e.*, *towards* the heart, so as to prevent any movement of blood backward. They are commonly placed in pairs, at various distances in different veins, but almost uniformly in each (fig. 229). In the smaller veins single valves are often met with; and three or four are sometimes placed together, or near one another, in the largest veins, such as the subclavian, at their junction with the jugular veins. The valves are semilunar; the unattached edge is in some examples concave, in others straight. They are composed of an outgrowth of the subendothelial tissue covered with endothelium. Their situation in the superficial veins of the forearm is readily discovered by pressing along their surface, in the direction opposite to the venous current, *i.e.*, from the elbow towards the wrist; when little swellings (fig. 229, C) appear in the position of each pair of valves. These swellings at once disappear when the pressure is removed.

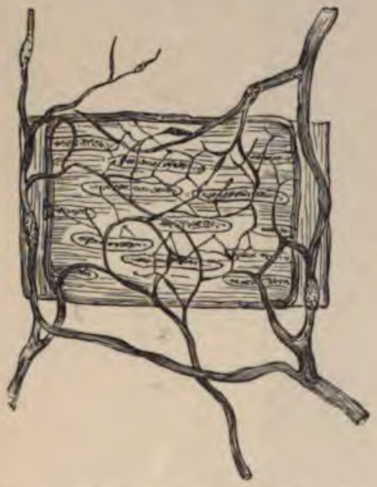

FIG. 227.—Ramification of nerves and termination in the muscular coat of a small artery of the frog. (Arnold.)

Valves are not equally numerous in all veins, and in many they are absent altogether. They are most numerous in the veins of the extremities, and more so in those of the leg than the arm. They are commonly *absent* in veins of less than a line in diameter, and, as a general rule, there are few or none in those which are not subject to muscular pressure. Among those veins which have no valves may be mentioned the superior and inferior vena cava, the pulmonary veins, the veins in the interior of the cranium and vertebral column, the veins of bone, and the umbilical vein. The valves of the portal tributaries are very inefficient.

Lymphatics of Arteries and Veins.—Lymphatic spaces are present in the coats of both arteries and veins. In the external coat of large vessels they form a plexus of more or less tubular vessels. In smaller vessels they appear as spaces lined by endothelium. Sometimes, as in the arteries of the omentum, mesentery, and membranes of the brain, in the pulmonary, hepatic, and splenic arteries, the spaces are continuous with vessels which distinctly ensheath them—*perivascular lymphatics* (fig. 231).

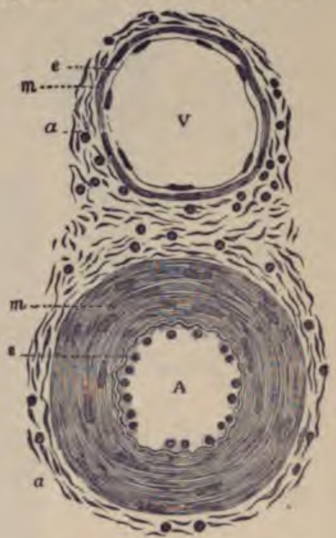

FIG. 228.—Transverse section through a small artery and vein of the mucous membrane of a child's epiglottis; the artery is thick-walled and the vein thin-walled. A. Artery, the letter is placed in the lumen of the vessel, *e*. Endothelial cells with nuclei clearly visible; these cells appear very thick from the contracted state of the vessel. Outside it a double wavy line marks the elastic layer of the tunica intima. *m*. Tunica media, consisting of unstriped muscular fibres circularly arranged; their nuclei are well seen. *a*. Part of the tunica adventitia showing bundles of connective-tissue fibre in section, with the circular nuclei of the connective-tissue corpuscles. This coat gradually merges into the surrounding connective tissue. V. In the lumen of the vein. The other letters indicate the same as in the artery. The muscular coat of the vein (*m*) is seen to be much thinner than that of the artery. × 350. (Klein and Noble Smith.)

The Capillaries.

In all vascular textures except some parts of the corpora cavernosa of the penis, of the uterine placenta, and of the spleen, the transmission of the blood from the minute branches of the arteries to the minute veins is affected through a network of capillaries.

Their walls are composed of endothelium—a single layer of elongated flattened and nucleated cells, so joined and dovetailed together as to form a continuous transparent membrane (fig. 232). Here and there the endothelial cells do not fit quite accurately; the space is filled up with cement material; these spots are called *pseudo-stomata*.

The *diameter* of the capillary vessels varies somewhat in the different tissues of the body, the most common size being about $\frac{1}{3000}$th of an inch (12 μ). Among the smallest may be mentioned those of the brain, and of the follicles of the mucous membrane of the intestines; among the largest, those of the skin, lungs, and especially those of the medulla of bones.

The *size* of capillaries varies necessarily in different animals in relation to the size of their blood corpuscles: thus, in the Proteus, the capillary circulation can just be discerned with the naked eye.

The *form* of the capillary network presents considerable variety in the different tissues of the body: the varieties consist principally of modifications of two chief kinds of mesh, the rounded and the elongated. That kind in which the meshes or interspaces have a roundish or polygonal form is the most common, and prevails in those parts in which the capillary network is most dense, such as the lungs (fig. 233), most glands and mucous membranes, and the cutis. The capillary network with elongated meshes is observed in parts in which the vessels are arranged among bundles of fine tubes or fibres, as in muscles and nerves. In such parts, the meshes form parallelograms (fig. 234), the short sides of which may be from three

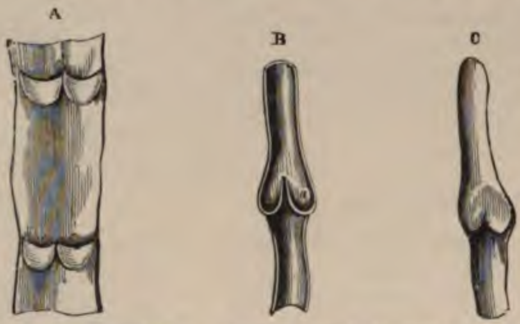

FIG. 229.—Diagram showing valves of veins. A, part of a vein laid open and spread out, with two pairs of valves. B, longitudinal section of a vein, showing the apposition of the edges of the valves in their closed state. C, portion of a distended vein, exhibiting a swelling in the situation of a pair of valves.

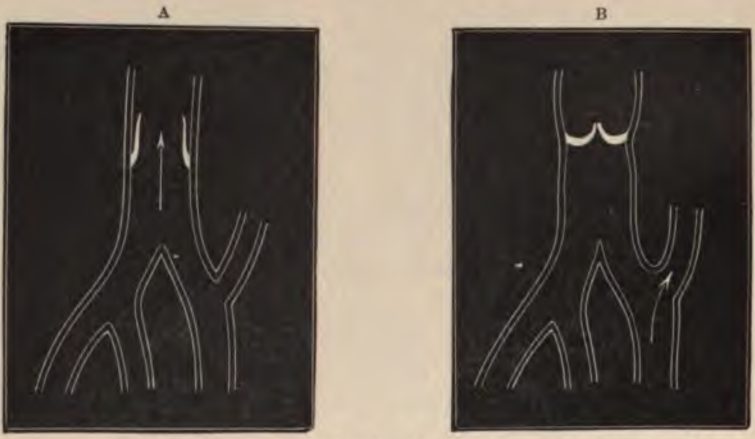

FIG. 230.—A, vein with valves open. B, with valves closed; stream of blood passing off by lateral channel. (Dalton.)

to eight or ten times less than the long ones; the long sides are more or less parallel to the long axis of the fibres.

The *number* of the capillaries and the *size of the meshes* in different parts determine in general the degree of *vascularity* of those parts. The capillary network is closest in the lungs and in the choroid coat of the eye.

It may be held as a general rule, that the more active the functions of an organ are, the more vascular it is. Hence the narrowness of the interspaces in all glandular organs, in mucous membranes, and in growing parts, and their much greater width in bones, ligaments, and other comparatively inactive tissues.

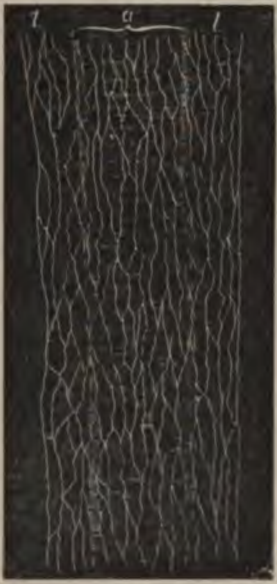

FIG. 231.—Surface view of an artery from the mesentery of a frog, ensheathed in a perivascular lymphatic vessel. *a*, the artery, with its circular muscular coat (media) indicated by broad transverse markings, with an indication of the adventitia outside. *l*, lymphatic vessel; its wall is a simple endothelial membrane. (Klein and Noble Smith.)

Lymphatic Vessels.

The blood leaves the heart by the arteries; it returns to the heart by the veins; but this last statement requires modification, for in the capillaries some of the blood-plasma escapes into the cell spaces of the tissues and nourishes the tissue-elements. This fluid, which is called *lymph*, is gathered up and carried back again into the blood by a system of vessels called *lymphatics*.

The principal vessels of the lymphatic system are, in structure, like small thin-walled veins, provided with numerous valves. The beaded appearance of the lymphatic vessels shown in figs. 236 and 237 is due to the presence of these valves. They commence in fine microscopic *lymph-capillaries*, in the organs and tissues of the body, and they end in two trunks which open into the large veins near the heart (fig. 235). The fluid which they contain, unlike the blood, passes only in one direction, namely, from the fine branches to the trunk, and so to the large veins, on entering which it is mingled with the stream of blood. In fig. 235 the greater part of the contents of

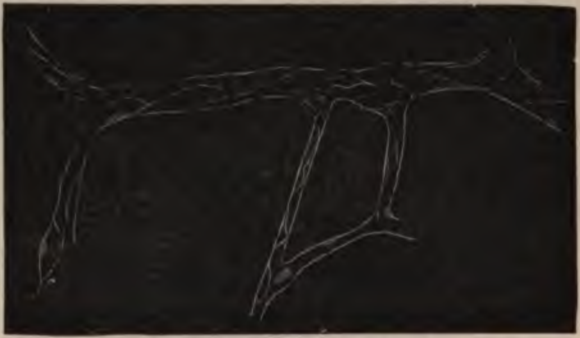

FIG. 232.—Capillary blood-vessels from the omentum of rabbit, showing the nucleated endothelial membrane of which they are composed. (Klein and Noble Smith.)

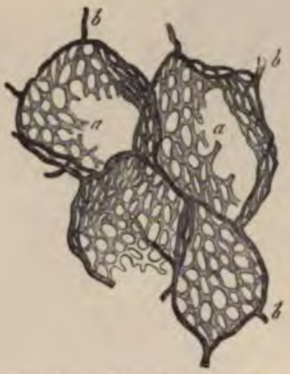

FIG. 233.—Network of capillary vessels of the air-cells of the horse's lung magnified. *a*, *a*, capillaries proceeding from *b*, *b*, terminal branches of the pulmonary artery. (Frey.)

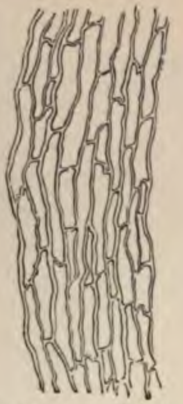

FIG. 234.—Injected capillary vessels of muscle seen with a low magnifying power. (Sharpey.)

the lymphatic system of vessels will be seen to pass through a comparatively large trunk called the *thoracic duct*, which finally empties its contents into the blood-stream, at the junction of the internal jugular and subclavian veins of the left side. There is a smaller duct on the right side. The lymphatic vessels of the intestinal canal are called *lacteals*, because during digestion (especially of a meal containing fat) the fluid contained in them resembles milk in appearance; and the *lymph* in the lacteals during the period of digestion is called *chyle*. Chyle is lymph containing finely divided fat-globules. In some parts of its course the lymph-stream passes through *lymphatic glands*, to be described later on.

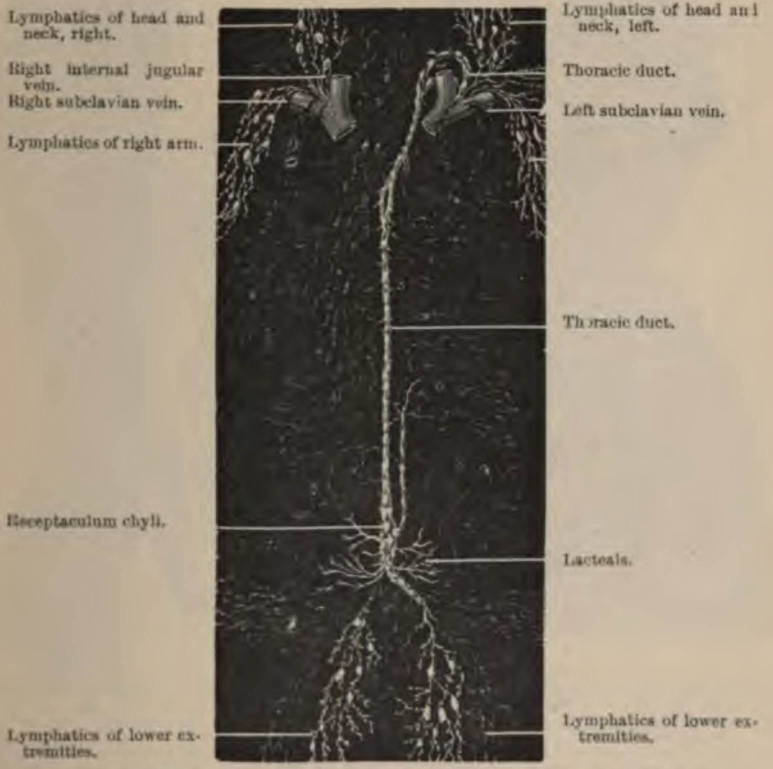
Lymphatics of head and neck, right.
Right internal jugular vein.
Right subclavian vein.
Lymphatics of right arm.
Receptaculum chyli.
Lymphatics of lower extremities.
Lymphatics of head and neck, left.
Thoracic duct.
Left subclavian vein.
Thoracic duct.
Lacteals.
Lymphatics of lower extremities.

FIG. 235.—Diagram of the principal groups of lymphatic vessels. (From Quain.)

Origin of Lymph Capillaries.—The lymphatic capillaries commence most commonly either (*a*) in closely-meshed networks, or (*b*) in irregular lacunar spaces between the various structures of which the different organs are composed. In serous membranes, such as the mesentery, they occur as a connected system of very irregular branched spaces partly occupied by connective-tissue corpuscles, and in these and other varieties of connective tissue, the cell spaces communicate freely with regular lymphatic vessels. In many cases,

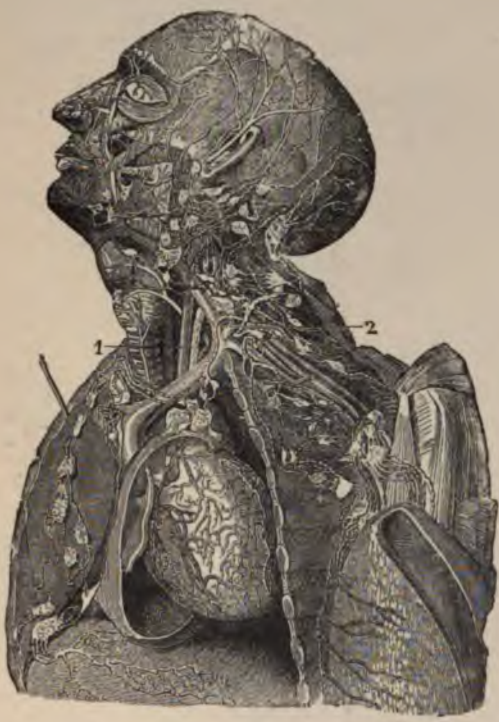

FIG. 236.—Lymphatic vessels of the head and neck and the upper part of the trunk (Mascagni). $\frac{1}{6}$.—The chest and pericardium have been opened on the left side, and the left mamma detached and thrown outwards over the left arm, so as to expose a great part of its deep surface. The principal lymphatic vessels and glands are shown on the side of the head and face and in the neck, axilla, and mediastinum. Between the left internal jugular vein and the common carotid artery, the upper ascending part of the thoracic duct marked 1, and above this, and descending to 2, the arch and last part of the duct. The termination of the upper lymphatics of the diaphragm in the mediastinal glands, as well as the cardiac and the deep mammary lymphatics, is also shown.

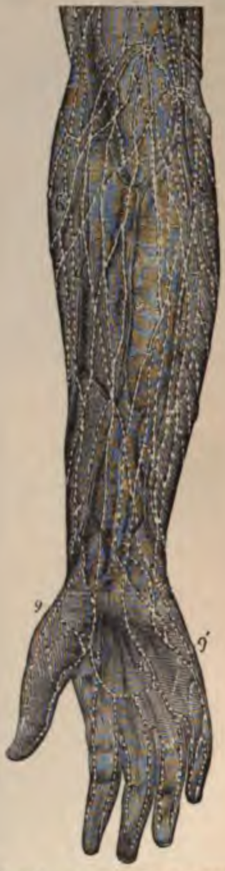

FIG. 237.—Superficial lymphatics of the forearm and palm of the hand. $\frac{1}{4}$.—5. Two small glands at the bend of the arm. 6. Radial lymphatic vessels. 7. Ulnar lymphatic vessels. 8, 8′. Palmar arch of lymphatics. 9, 9′. Outer and inner sets of vessels. *b*. Cephalic vein. *d*. Radial vein. *e*. Median vein. *f*. Ulnar vein. The lymphatics are represented as lying on the deep fascia. (Mascagni.)

though they are formed mostly by the chinks and crannies between the parts which may happen to form the framework of the organ in which they exist, they are lined by a distinct layer of endothelium.

The lacteals offer an illustration of another mode of origin, namely, as blind dilated extremities in the villi of the small intestine (see fig. 38, p. 27).

Structure of Lymph Capillaries.—The structure of lymphatic capillaries is very similar to that of blood capillaries; their walls consist of a single layer of elongated endothelial cells with sinuous outline, which cohere along their edges to form a delicate membrane. They differ from blood capillaries mainly in their larger and very variable calibre, and in their numerous communications with the spaces of the lymph-canalicular system.

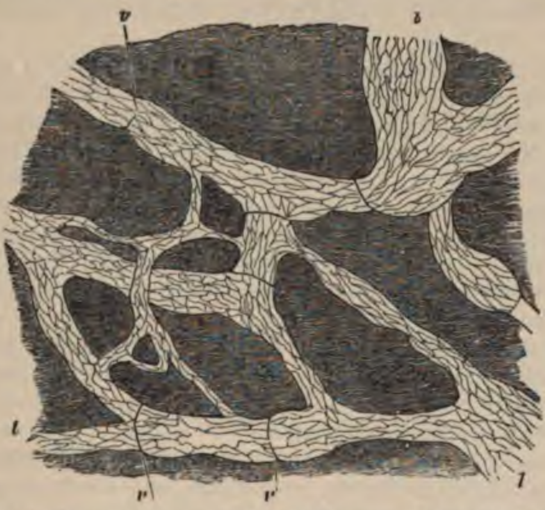

FIG. 238.—Lymphatics of central tendon of rabbit's diaphragm, stained with silver nitrate. The shaded background is composed of bundles of white fibres, between which the lymphatics lie. *l*, Lymphatics lined by long narrow endothelial cells, and showing *v* valves at frequent intervals. (Schofield.)

In certain parts of the body, *stomata* exist, by which lymphatic capillaries directly communicate with parts formerly supposed to be closed cavities. They have been found in the pleura, and in other serous membranes; a serous cavity thus forms a large lymph-sinus or widening out of the lymph-capillary system with which it directly communicates.

A very typical plexus of lymphatic capillaries is seen in the central tendon of the diaphragm. Fig. 238 represents the appearance presented after staining with silver nitrate.

CHAPTER XIX

THE CIRCULATION OF THE BLOOD

WE have now to approach the physiological side of the subject, and study the means by which the blood is kept in movement, so that it may convey nutriment to all parts, and remove from those parts the waste products of their activity.

Previous to the time of Harvey, the vaguest notions prevailed regarding the use and movements of the blood. The arteries were supposed by some to contain air, by others to contain a more subtle essence called animal spirits; the animal spirits were supposed to start from the ventricles of the brain, and they were controlled by the soul which was situated in the pineal gland. How the animal spirits got into the arteries was an anatomical detail which was bridged across by the imagination.

There was an idea that the blood moved, but this was considered to be a haphazard, to-and-fro movement, and confined to the veins. The proofs that the movement is in a circle were discovered by William Harvey, and to this eminent discoverer also belongs the credit of pointing out the methods by which every physiological problem must be studied. In the first place there must be correct anatomical knowledge, and in the second there must be experiment, by which deductions from structure can be tested; moreover, this second method is by far the more important of the two. Harvey's proofs of the circulation came under both these heads. The structural or anatomical facts upon which he relied were the following:—

1. The existence of two distinct sets of tubes in connection with the heart, namely, the arteries and the veins.

2. The existence in the heart and also in the veins, of valves which would only allow the passage of the blood in one direction.

His experimental facts were the following:—

3. That the blood spurts with great force and in a jerky manner from an artery opened during life, each jerk corresponding with a beat of the heart.

4. That if the large veins near the heart are tied, the heart becomes pale, flaccid, and bloodless, and on removal of the ligature the blood again flows into the heart.

5. If the aorta is tied, the heart becomes distended with blood, and cannot empty itself until the ligature is removed.

6. The preceding experiments were performed on animals, but by the following experiment he showed that the circulation is a fact in man also; if a ligature is drawn tightly round a limb, no blood can enter it, and it becomes pale and cold. If the ligature is somewhat relaxed so that blood can enter but cannot leave the limb, it becomes swollen. If the ligature is removed, the limb soon regains its normal appearance.

7. Harvey also drew attention to the fact that there is general constitutional disturbance resulting from the introduction of a poison at a single point, and that this can only be explained by a movement of the circulating fluid all over the body.

Since Harvey's time many other proofs have accumulated; for instance:—

8. If an artery is wounded, hæmorrhage may be stopped by pressure applied between the heart and the wound; but in the case of a wound in a vein, the pressure must be applied beyond the seat of injury.

9. If a substance which, like ferrocyanide of potassium, can be readily detected, is injected at a certain point into a blood-vessel, it will after the lapse of a short interval have entirely traversed the circulation and be found in the blood collected from the same point.

10. Perhaps the most satisfactory proof of the circulation is one now within the reach of every student, though beyond that of Harvey. It consists in actually seeing the passage of the blood from small arteries through capillaries into veins in the transparent parts of animals, such as the tail of a tadpole or the web of a frog's foot. Harvey could not follow this part of the circulation, for he had no lenses sufficiently powerful to enable him to see it. Harvey's idea of the circulation here was that the arteries carried the blood to the tissues, which he considered to be of the nature of a sponge, and the veins collected the blood again, much in the same way as drainage pipes would collect the water of a swamp. The discovery that the ends of the arteries are connected to the commencements of veins by a definite system of small tubes we now call capillaries, was made by Malpighi, in the year 1661. He first observed them in the tail of the tadpole, and Leeuwenhoek, seven years later, saw the circulation in the lung of the frog.

We can now proceed to study some of the principles on which the circulation depends:—

The simplest possible way in which we could represent the circulatory system is shown in fig. 239 A. Here there is a closed ring containing fluid, and upon one point of the tube is an enlargement (H) which will correspond to the heart. It is obvious that if such a ring made of an ordinary Higginson's syringe and a tube were placed upon the table, there would be no movement of the fluid in it; in order to make the fluid move there must be a difference of pressure between different parts of the fluid, and this difference of pressure is caused in the fluid by the pressure on it of the heart walls. If, for instance, one takes the syringe in one's hand and squeezes it, one imitates a contraction of the heart: if the syringe has no valves, the fluid would pass out of each end of it in the direction of the two arrows placed outside the ring. When the pressure on the syringe is relaxed (this would correspond to the interval between the heart beats), the fluid would return into the heart again in the direction of the two arrows placed inside the ring.

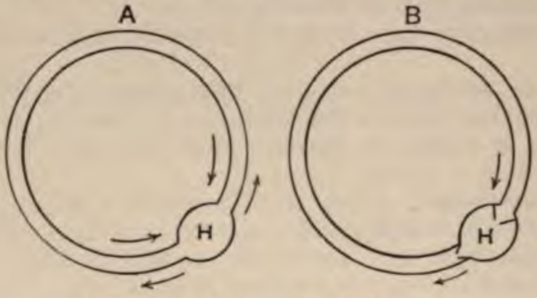

FIG. 239.—Simple schema of the circulation.

This, however, would be merely a to-and-fro movement, not a circulation. Fig. 239 B shows how this to-and-fro movement could, by the presence of valves, be converted into a circulation; when the heart contracts the fluid could pass only in the direction of the outer arrow; when the heart relaxes it could pass only in the direction of the inner arrow; the direction of both arrows is the same, and so if the contraction and relaxation of the heart are repeated often enough the fluid will move round and round within the tubular ring.

The main factor in the circulation is difference of pressure. In general terms fluid flows from where the pressure is high to where it is lower. This difference of pressure is produced in the first instance by the contraction of the heart, but we shall find in our study of the vessels that some of this pressure is stored up in the elastic arterial walls, and keeps up the circulation during the periods that the heart is resting.

Coming to different groups in the animal kingdom we may take the crayfish or the lobster as instances of animals which possess a hæmolymph system, that is, there is no distinction between blood and lymph. The heart pumps the circulating fluid along a system of vessels which distribute it over the body; there are no capillaries, and the hæmolymph is discharged into the tissue spaces; it is thence drained into channels which convey it to the gills, and after it is aërated there in a set of irregular vessels, it is returned to the pericardium. It is sucked from the pericardium into the heart during diastole, through five small orifices in the cardiac wall; during systole these are closed by valves. In these animals the rate of flow of hæmolymph is necessarily slow.

In worms, the circulatory system is almost as simple as in the schema just described; the heart is a long contractile tube provided with valves, which contracts peristaltically and presses the blood forwards into the aorta at its anterior end; this divides into arteries for the supply of the body; the blood passes through these to capillaries, and is collected by veins which converge to one or two main trunks that enter the heart at its posterior end.

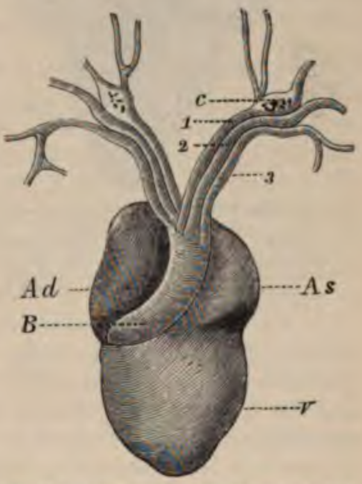

FIG. 240.—The heart of a frog (Rana esculenta) from the front. *V*, ventricle; *Ad*, right auricle; *As*, left auricle; *B*, bulbus arteriosus, dividing into right and left aortæ. (Ecker.)

In fishes, the heart is divided into a number of chambers placed in single file, one in front of the other; the most posterior which receives the veins is called the sinus venosus; this contracts and forces the blood into the next chamber, called the auricle; this forces the blood into the next cavity, that of the ventricle, and last of all is the aortic bulb. From the bulb, branches pass to the gills, where they break up into capillaries, and the blood is aërated: it then once more enters larger vessels which unite to form the dorsal aorta, whence the blood is distributed by arteries to all parts of the body; here it enters the systemic capillaries, then the veins which enter the sinus (whence we started) by a few large trunks.

Taking the frog as an instance of an amphibian, we find the heart more complex, and the simple peristaltic action of the heart muscle as we have described it in the hearts of worm and fish, becomes correspondingly modified. There is only one ventricle, but there are two auricles, right and left.

The ventricle contains mixed blood, since it receives arterial blood from the left auricle (which is the smaller of the two), and venous blood from the right auricle; the right auricle receives the venous blood from the sinus, which in turn receives it from the systemic veins. The left auricle, as in man, receives the blood from the pulmonary veins.

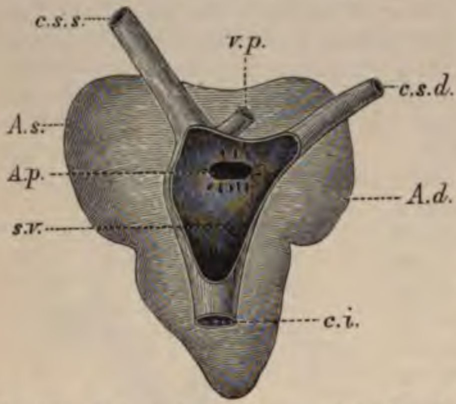

FIG. 241.—The heart of a frog (Rana esculenta) from the back. *s.v.*, sinus venosus opened; *c.s.s.*, left vena cava superior; *c.s.d.*, right vena cava superior; *c.i.*, vena cava inferior; *v.p.*, vena pulmonalis; *A.d.*, right auricle; *A.s.*, left auricle; *A.p.*, opening of communication between the right auricle and the sinus venosus. × 2½—3. (Ecker.)

When the ventricle contracts, it forces the blood onward into the aortic bulb which divides into branches on each side for the supply of the head (fig. 240, 1), lungs and skin (fig. 240, 3), and the third branch (fig. 240, 2), unites with its fellow of the opposite side to form the dorsal aorta for the supply of the rest of the body.

Passing from the amphibians to the reptiles, we find the division of the ventricle into two beginning, but it is not complete till we reach the birds. The heart reaches its fullest development in mammals, and we have already described the human as an example of the mammalian heart. The sinus venosus is not present as a distinct chamber in the mammalian heart, but is represented by that portion of the right auricle at which the large veins enter.

CHAPTER XX

PHYSIOLOGY OF THE HEART

The Cardiac Cycle.

THE series of changes that occur in the heart constitutes the *cardiac cycle.* This must be distinguished from the course of the circulation. The term cycle indicates that if one observes the heart at any particular moment, the heart from that moment onwards undergoes certain changes until it once more assumes the same condition that it had at the moment when the observation commenced, when the cycle is again repeated, and so on. This series of changes consists of alternate contraction and relaxation. Contraction is known as **systole**, and relaxation as **diastole.**

The contraction of the two auricles takes place simultaneously, and constitutes the *auricular systole;* this is followed by the simultaneous contraction of the two ventricles, *ventricular systole,* and that by a period during which the whole of the heart is in a state of relaxation or *diastole;* then the cycle again commences with the auricular systole.

Taking 72 as the average number of heart beats per minute, each cycle will occupy $\frac{1}{72}$ of a minute, or a little more than 0·8 of a second. This may be approximately distributed in the following way:—

Auricular systole	about 0·1	+	Auricular diastole	0·7	=	0·8
Ventricular systole	,, 0·3	+	Ventricular diastole	0·5	=	0·8
Total systole	,, 0·4	+	Joint diastole	0·4	=	0·8

If the speed of the heart is quickened, the time occupied by each cycle is diminished, but the diminution affects chiefly the diastole. These different parts of the cycle must next be studied in detail.

The Auricular Diastole.—During this time, the blood from the large veins is flowing into the auricles, the pressure in the veins though very low being greater than that in the empty auricles. The blood expands the auricles, and during the last part of the auricular diastole it passes on into the ventricles. The dilatation of the auricles is assisted by the elastic traction of the lungs. The lungs being in a closed cavity, the thorax, and being distended with air, are in virtue of their elasticity always tending to recoil and squeeze the air out of their interior; in so doing they drag upon any other organ with which their surface is in contact: this elastic traction will be greatest when the lungs are most distended, that is during inspiration, and will be more felt by the thin-walled auricles than by the thick-walled ventricles of the heart.

The Auricular Systole is sudden and very rapid; by contracting, the auricles empty themselves into the ventricles. The contraction commences at the entrance of the great veins, and is thence propagated towards the auriculo-ventricular opening. The reason why the blood does not pass backwards into the veins, but onward into the ventricles, is again a question of pressure; the pressure in the relaxed ventricles, which is so small as to exert a suction action on the auricular blood, is less than in the veins. Moreover, the auriculo-ventricular orifice is large and widely dilated, whereas the mouths of the veins are constricted by the contraction of their muscular coats. Though there is no regurgitation of the blood backwards into the veins, there is a stagnation of the flow of blood onwards to the auricles. The veins have no valves at their entrance into the auricles, except the coronary vein which does possess a valve; there are valves, however, at the junction of the subclavian and internal jugular veins.

Ventricular Diastole; during the last part of the auricular diastole and the whole of the auricular systole, the ventricles have been relaxed and then filled with blood. The dilatation of the ventricles is chiefly brought about in virtue of their elasticity; this is particularly evident in the left ventricle with its thick muscular coat. It is equal to 23 mm. of mercury, and is quite independent of the elastic traction of the lungs, which, however, in the case of the thinner-walled right ventricle comes into play.

The Ventricular Systole; this is the contraction of the ventricles, and it occupies more time than the auricular systole; when it occurs the auriculo-ventricular valves are closed and prevent regurgitation into the auricles, and when the force of the systole is greatest, and the pressure within the ventricles exceeds that in the large arteries which originate from them, the semilunar valves are opened, and the ventricles empty themselves, the left into the aorta, the right into the pulmonary artery. Each ventricle ejects about 3 ounces of blood with each contraction; the left in virtue of its thicker walls acts much more forcibly than the right. The greater force of the left ventricle is necessary, as it has to overcome the resistance of the small vessels all over the body; whereas the right ventricle has only to overcome peripheral resistance in the pulmonary district.

The shape of both ventricles during systole has been described as undergoing an alteration, the diameters in the plane of the base being diminished, and the length of the ventricles slightly lessened. The whole heart, moreover, moves towards the right and forwards, twisting on its long axis and exposing more of the left ventricle anteriorly than when it is at rest. These movements, which were first described by Harvey, have been since Harvey's time believed to be the cause of the cardiac impulse or apex beat which is to be felt in the fifth intercostal space about three inches from the middle line. It has, however, been shown by Haycraft that these changes only occur when the chest walls are open. When the heart contracts in a closed thorax it undergoes no rotation, and the contraction is concentric, that is, equal in all directions. The diminution of the heart's volume which occurs in systole cannot be the cause of the apex beat; it would rather tend to draw the chest wall inwards than push it outwards.

The apex beat is caused by two changes in the physical condition of the heart. In the first place, on systole the heart becomes hard and tense, and secondly, its attachment to the aorta becomes rigid instead of being flexible as it is in diastole. Thus, in systole, the heart becomes rigidly fixed to the aorta, and, as this vessel is curved, it tends to open out into a straight line, but is prevented by the counter-resistance at the two ends of the arch. These are (*a*) the resistance of the chest wall against the heart, and (*b*) that of the vertebræ and ribs against the thoracic aorta. The pressure of the heart against the chest wall is confined to a small area, situated in the fifth intercostal space, because the heart surface is much more curved than the internal thoracic wall. The forward movement this pressure causes is the apex beat. It must be noted that this movement is not over the actual apex of the heart, but is communicated from an area on the anterior cardiac surface.

Action of the Valves of the Heart.

1. *The Auriculo-Ventricular.*—The distension of the ventricles with blood continues throughout the whole period of their diastole. The auriculo-ventricular valves are gradually brought into place by some of the blood getting behind the cusps and floating them up; by the time that the diastole is complete, the valves are in apposition, and they are firmly closed by the reflux current caused by the systole of the ventricles. The diminution in the size of the auriculo-ventricular rings which occur during systole, renders the auriculo-ventricular valves competent to close these openings. The margins of the cusps of the valves are still more secured in apposition with one another, by the simultaneous contraction of the musculi papillares, whose chordæ tendineæ have a special mode of attachment for this object. The cusps of the auriculo-ventricular valves meet not by their edges only, but by the opposed surfaces of their thin outer borders.

The musculi papillares prevent the auriculo-ventricular valves from being everted into the auricle. For the chordæ tendineæ might allow the valves to be pressed back into the auricle, were it not that when the wall of the ventricle is brought by its contraction nearer the auriculo-ventricular orifice, the musculi papillares more than compensate for this by their own contraction; they hold the cords diastole it passes on into the ventricles. The dilatation of the auricles is assisted by the elastic traction of the lungs. The lungs being in a closed cavity, the thorax, and being distended with air, are in virtue of their elasticity always tending to recoil and squeeze the air out of their interior; in so doing they drag upon any other organ with which their surface is in contact: this elastic traction will be greatest when the lungs are most distended, that is during inspiration, and will be more felt by the thin-walled auricles than by the thick-walled ventricles of the heart.

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These statements apply equally to the auriculo-ventricular valves on both sides of the heart; the closure of both is generally complete every time the ventricles contract. But in some circumstances the tricuspid valve does not completely close, and a certain quantity of blood is forced back into the auricle. This has been called its *safety-valve action*. The circumstances in which it usually happens are those in which the vessels of the lung are already completely full when the right ventricle contracts, as, *e.g.*, in certain pulmonary diseases, and in very active muscular exertion. In these cases, the tricuspid valve does not completely close, and the regurgitation of the blood may be indicated by a pulsation in the jugular veins synchronous with that in the carotid arteries.

2. *The Semilunar Valves.*—The commencement of the ventricular systole precedes the opening of the aortic valves by a fraction of a second, as is proved by examining records of the intraventricular and aortic pressure curves taken simultaneously. The first result of the contraction of the ventricles is the closure of the auriculo-ventricular valves, and as soon as this has been effected the intraventricular pressure begins to rise. It quickly reaches a point at which it equals the aortic pressure, and then exceeds it, and as soon as this pressure difference has been established the aortic valves are opened and blood flows from the ventricle into the aorta. The valves are kept open as long as the intra-ventricular pressure exceeds the aortic, but as soon as the heart has emptied itself, the ventricle begins to relax, its internal pressure consequently begins to fall, and an instant is quickly reached at which it is exceeded by the aortic. The blood, therefore, tends to flow back from the aorta, and in so doing fills up the pockets of the semilunar valves, which have always remained partly filled, and brings them together with a sharp movement. The movements of the valves are therefore effected by the occurrence of differences of pressure upon their two faces. When they meet they completely close the orifice, because their inner edges, which are thinner than the rest of the valves, are brought into apposition and held so by the high pressure acting on their aortic surfaces only.

The Sounds of the Heart.

When the ear is placed over the region of the heart, two *sounds* may be heard at every beat of the heart, which follow in quick succession, and are succeeded by a *pause* or period of silence. The *first* or *systolic* sound is dull and prolonged; its commencement coincides with the impulse of the heart against the chest wall, and just precedes the pulse at the wrist. The *second* or *diastolic* sound is shorter and sharper, with a somewhat flapping character, and follows close after the arterial pulse. The periods of time occupied respectively by the two sounds taken together and by the pause, are nearly equal. Thus, according to Walshe, if the cardiac cycle be divided into tenths, the first sound occupies $\frac{4}{10}$; the second sound, $\frac{2}{10}$; the first pause (almost imperceptible), $\frac{1}{10}$; and the second pause, $\frac{3}{10}$. The sounds are often but somewhat inaptly compared to the syllables, *lūbb—dŭp*.

The events which correspond, in point of time, with the *first* sound, are (1) the contraction of the ventricles, (2) the first part of the dilatation of the auricles, (3) the tension of the auriculo-ventricular valves, (4) the opening of the semilunar valves, and (5) the propulsion of blood into the arteries. The sound is succeeded, in about one-thirtieth of a second, by the pulsation of the facial arteries, and in about one-sixth of a second, by the pulsation of the arteries at the wrist. The *second* sound, in point of time, immediately follows the cessation of the ventricular contraction, and corresponds with (*a*) the tension of the semilunar valves, (*b*) the continued dilatation of the auricles, (*c*) the commencing dilatation of the ventricles, and (*d*) the opening of the auriculo-ventricular valves. The *pause* immediately follows the second sound, and corresponds *in its first part* with the completed distension of the auricles, and *in its second* with their contraction, and the completed distension of the ventricles; the auriculo-ventricular valves are open, and the arterial valves closed during the whole of the pause.

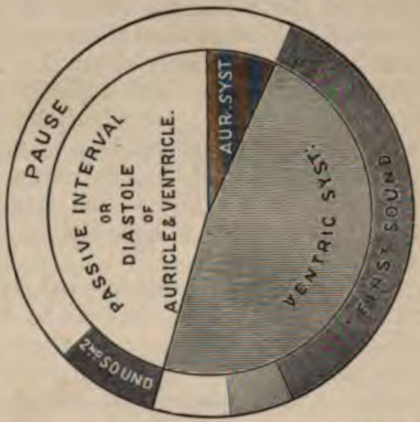

FIG. 242.—Scheme of cardiac cycle. The inner circle shows the events which occur within the heart; the outer the relation of the sounds and pauses to these events. (Sharpey and Gairdner.)

Causes.—The exact cause of the first sound of the heart is a matter of discussion. Two factors probably enter into it, viz., first, the *vibration of the auriculo-ventricular valves and the chordæ tendineæ.* This vibration is produced by the increased intraventricular pressure set up when the ventricular systole commences, which puts the valves on the stretch. It is not unlikely, too, that the vibration of the ventricular walls themselves, and of the aorta and pulmonary artery, all of which parts are suddenly put into a state of tension at the moment of ventricular contraction, may have some part in producing the first sound. Secondly, *the muscular sound* produced by contraction of the mass of muscular fibres which forms the ventricle. Looking upon the contraction of the heart as a single contraction and not as a series of contractions or tetanus, it is at first sight difficult to see why there should be any muscular sound at all when the heart contracts, as a single muscular contraction does not produce sound. It has been suggested, however, that it arises from the repeated unequal tension produced when the wave of muscular contraction passes along the very intricately arranged fibres of the ventricular walls. Many regard the valvular element is the more important of the two factors, because the sound is loudest at first, when the vibration of the valves commences, and fades away as the vibrations cease. If the sound was mainly muscular, it would be loudest when the muscular contraction was most powerful, which is approximately about the middle of the ventricular systole. The facts of disease lend support to the theory that the first sound is mainly valvular; for when the valves are incompetent, the first sound is largely replaced by a murmur due to regurgitation of blood into the auricle. After the removal of the heart from the body, the muscular contribution to the first sound is audible, but it is very faint. It is stated to have a somewhat lower pitch than the valvular sound.

There is, on the other hand, much to be said against the view that the cause of the first sound is entirely or even largely due to vibration of the auriculo-ventricular valves. Any sound produced by the valves must be very quickly damped by the high pressure acting on their ventricular surfaces only. The sustained character of the sound (throughout practically the whole of the ventricular systole) is on the other hand exactly what is to be expected if it is of muscular origin. The argument that the extent to which the muscle sound contributes to the production of the first sound can be judged from the sound heard in an isolated and empty heart is quite fallacious, since under these conditions the muscle is contracting against no resistance.

The cause of the *second* sound is more simple than that of the first. It is entirely due to the vibration consequent on the sudden stretching of the semilunar valves when they are pressed down across the orifices of the aorta and pulmonary artery. The influence of these valves in producing the sound was first demonstrated by Hope, who experimented with the hearts of calves. In these experiments two delicate curved needles were inserted, one into the aorta, and another into the pulmonary artery, below the line of attachment of the semilunar valves, and, after being carried upwards about half an inch, were brought out again through the coats of the respective vessels, so that in each vessel one valve was included between the arterial walls and the wire. Upon applying the stethoscope to the vessels, after such an operation, the second sound ceased to be audible. Disease of these valves, when sufficient to interfere with their efficient action, also demonstrates the same fact by modifying the second sound or destroying its distinctness.

The contraction of the auricles is inaudible.

The first sound is heard most distinctly at the apex beat in the fifth interspace; the second sound is best heard over the second *right* costal cartilage—that is, the place where the aorta lies nearest to the surface. The pulmonary and aortic valves generally close simultaneously. In some cases, however, the aortic may close slightly before the pulmonary valves, giving rise to a "reduplicated second sound." The pulmonary contribution to this sound is best heard over the second *left* cartilage.

The Coronary Arteries.

The coronary arteries are the first branches of the aorta; they originate from the sinuses of Valsalva, and are destined for the supply of the heart itself; the entrance of the coronary vein, into the right auricle, we have already seen (p. 207).

Ligature of the coronary arteries causes almost immediate death; the heart, deprived of its normal blood-supply, beats irregularly, goes into fibrillary twitchings, and then ceases to contract altogether.

In fatty degeneration of the heart in man, sudden death is by no means infrequent. This is in many cases due to a growth in thickness of the walls of the coronary arteries called atheroma, which progresses until the lumen of these arteries is obliterated, and the man dies almost as if they had been ligatured.

Self-steering Action of the Heart.—This expression was originated by Brücke. He supposed that the semilunar valves closed the orifices of the coronary arteries during the systole of the heart. Unlike all the other arteries of the body, the coronary arteries would therefore fill only during diastole, and this increased fulness of the vessels in the heart walls during diastole would assist the ventricle to dilate. This, however, is incorrect; the valves do not cover the mouths of the arteries; and at the beginning of systole the velocity and pressure in the coronary arteries increase; but later on during systole the ventricular wall is so strongly contracted that the muscular tension becomes greater than the coronary pressure, and so the coronary arteries and their branches are compressed, and the blood driven back into the aorta; the coronary arteries are then again filled with the commencing diastole. Self-steering action of the heart therefore exists, but it is brought about in a different way from what Brücke supposed.

Cardiographs.

A cardiograph is an instrument for obtaining a graphic record of the heart's movements. In animals the heart may be exposed, and levers placed in connection with its various parts may be employed to write on a revolving blackened surface.

A simple instrument for the frog's heart is the following:—

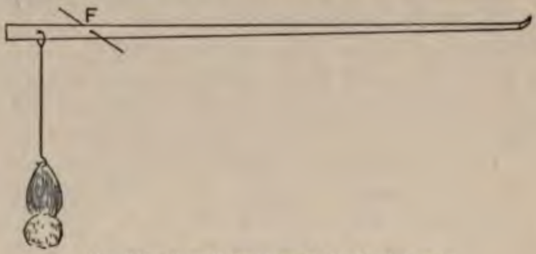

FIG. 243.—Simple Cardiograph for frog's heart.

The sternum of the frog having been removed, the pericardium opened, and the frænum (a small band from the back of the heart to the pericardium) divided, the heart is pulled through the opening, a minute hook placed in its apex, and this is fixed by a silk thread to a lever pivoted at F as in the figure. The cardiac wave of contraction starts at the sinus, this is followed by the auricular systole, and that by the ventricular systole and pause. This is recorded as in the next figure (fig. 244) by movements of the writing point at the end of the long arm of the lever. Such apparatus is, however, not applicable to the human heart, and all the various forms of cardiograph devised for this purpose are modifications of Marey's tambours. One of those most frequently used is depicted in the next two diagrams.

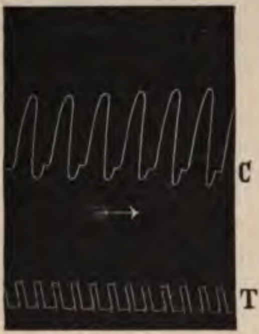

FIG. 244.—Cardiogram of frog's heart. C, showing auricular, followed by ventricular beat; T, time in half seconds.

It (fig. 245) consists of a cup-shaped metal box over the open front of which is stretched an elastic india-rubber membrane, upon which is fixed a small knob of hard wood or ivory. This knob, however, may be attached, as in the figure, to the side of the box by means of a spring, and may be made to act upon a metal disc attached to the elastic membrane.

The knob is for application to the chest-wall over the apex beat. The box or tambour communicates by means of an air-tight tube with the interior of a second tambour, in connection with which is a long and light lever. The shock of the heart's impulse being communicated to the ivory knob and through it to the first tambour, the effect is at once transmitted by the column of air in the elastic tube to the interior of the second tambour, also closed, and through the elastic and movable lid of the latter to the lever, which is placed in connection with a registering apparatus, which consists of a cylinder covered with smoked paper, revolving with a definite velocity. The point of the lever writes upon the paper, and a tracing of the heart's impulse or **cardiogram** is thus obtained.

Fig. 247 represents a typical tracing obtained in this way. The first small rise of the lever is caused by the auricular, the second larger rise by the ventricular systole; the downstroke represents the

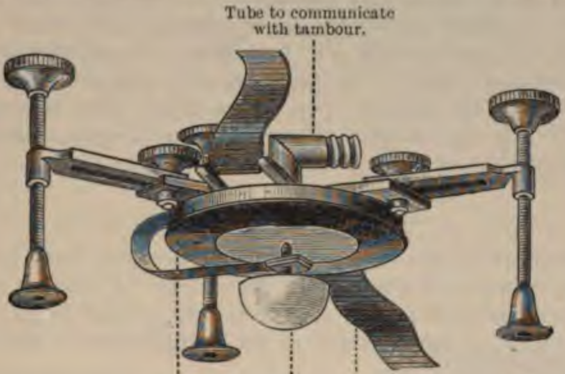
Tube to communicate with tambour.
Tambour.
Ivory knob.
Tape to attach the instrument to the chest.

FIG. 245.—Cardiograph. (Sanderson's.)

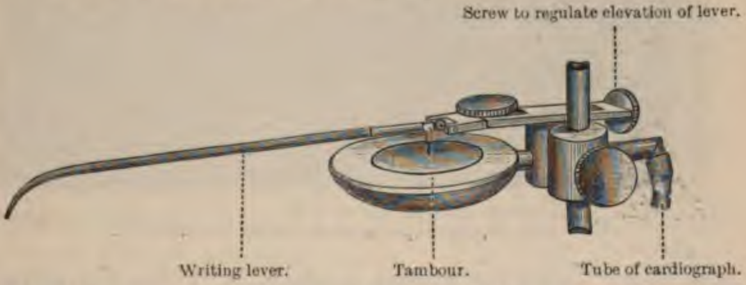

FIG. 246.—Marey's Tambour, to which the movement of the column of air in the first tambour is conducted by a tube, and from which it is communicated by the lever to a revolving cylinder, so that the tracing of the movement of the impulse beat is obtained.

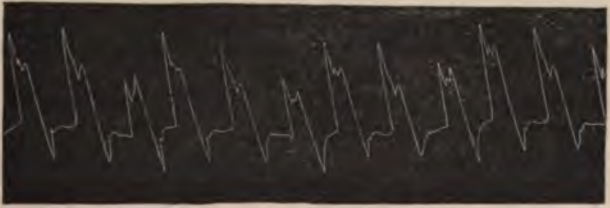

FIG. 247.—Cardiogram from human heart. The variations in the individual beats are due to the influence of the respiratory movements on the heart. To be read from left to right.

pause, the tremors at the commencement of which are partly instrumental and partly caused by the closure of the semilunar valves.

Another method of obtaining a tracing from one's own heart consists in dispensing with the first tambour, and placing the tube of the recording tambour in one's mouth, and holding the breath though keeping the glottis open. The chest then acts as the first tambour, and the movements of the lever (cardio-pneumatogram) may be written in the usual way.

Intracardiac Pressure.

The tracings of the cardiograph are, however, very variable, and their interpretation is a matter of discussion. A much better method of obtaining a graphic record of the events of the cardiac cycle consists in connecting the interior of an animal's heart with recording apparatus. There are several methods by which the intracardiac pressure may be recorded.

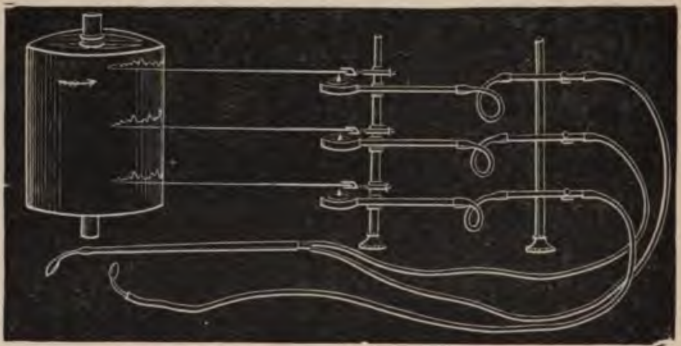

Fig. 248.—Apparatus of MM. Chauveau and Marey for estimating the variations of endocardiac pressure, and the production of the impulse of the heart.

By placing two small indiarubber air-bags or *cardiac sounds* down the jugular vein into the interior respectively of the right auricle and the right ventricle, and a third in an intercostal space in front of the heart of a living animal (horse), and placing these bags, by means of long narrow tubes, in communication with three tambours with levers, arranged one over the others in connection with a registering apparatus (fig. 248), Chauveau and Marey were able to record and measure the variations of the intracardiac pressure and the comparative duration of the contractions of the auricles and ventricles. By means of the same apparatus, the synchronism of the impulse with the contraction of the ventricles is also shown.

In the tracing (fig. 249), the intervals between the vertical lines represent periods of a tenth of a second. The parts on which any given vertical line falls represent simultaneous events. It will be seen that the contraction of the auricle, indicated by the marked curve at A in the first tracing, causes a slight increase of pressure in the ventricle, which is shown at A′ in the second tracing, and produces also a slight impulse, which is indicated by A″ in the third tracing. The closure of the semilunar valves causes a momentarily increased pressure in the ventricle at D′, affects the pressure in the auricle D, and is also shown in the tracing of the impulse, D″.*

The large curve of the ventricular and the impulse tracings, between A′ and D′, and A″ and D″, are caused by the ventricular contraction, while the smaller undulations, between B and C, B′ and C′, B″ and C″, are caused by the vibrations consequent on the tightening and closure of the auriculo-ventricular valves.

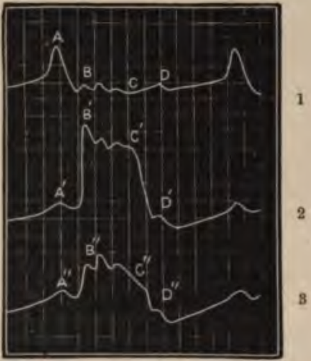

FIG. 249.—Tracings of (1), Intra-auricular, and (2), Intra-ventricular pressure, and (3), of the impulse of the heart; to be read from left to right; obtained by Chauveau and Marey's apparatus.

Much objection has, however, been taken to this method of investigation. First, because it does not admit of both positive and negative pressure being recorded. Secondly, because the method is only applicable to large animals, such as the horse. Thirdly, because the intraventricular changes of pressure are communicated to the recording tambour by a long elastic column of air; and fourthly, because the tambour arrangement has a tendency to record inertia vibrations. Rolleston re-investigated the subject with a more suitable but rather complicated apparatus. The principle of the method consisted in placing the cavity of a heart-chamber in communication with a recording apparatus by means of a tube containing saline solution. His recording apparatus consisted of a lever connected to a piston; the upward and downward movements of the piston-rod were due to the varying pressures exerted on the blood by the contraction and dilatation of the heart; the rise and fall of the lever were controlled by the resistance to torsion of a steel ribbon to which it was attached. The following figure (fig. 250) shows the kind of tracing he obtained. He found:—

1. That there is no distinct and separate auricular contraction marked in the curves obtained from either right or left ventricles,

---

* There can be no doubt that the point D which Marey considered to coincide with the closure of the semilunar valves does not really do so. The closure occurs much earlier (E in fig. 252).

the auricular and ventricular rises of pressure being merged into one continuous rise.

2. That the auriculo-ventricular valves are closed before any great rise of intraventricular pressure above that which results from the auricular systole occurs (*a*, fig. 250). The closure of this valve does not produce any notch or wave.

3. That the semilunar valves open at the point in the ventricular systole, situated (at *c*) about or a little above the junction of the middle and upper third of the ascending line (A B), and the closure about the shoulder (D).

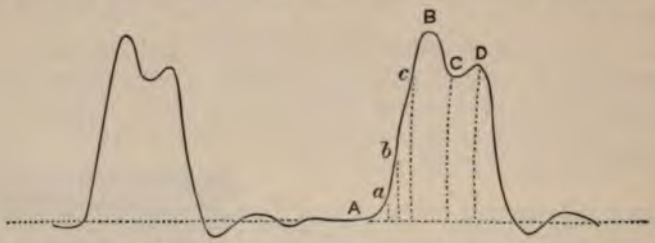

FIG. 250.—Curve from left ventricle obtained by Rolleston's apparatus; the abscissa shows atmospheric pressure.

4. That the minimum pressure in the ventricle may fall below that of the atmosphere, but that the amount varies considerably.

Another method of overcoming the imperfections of Marey's tambour is by the use of Hürthle's manometer (fig. 244). In this the tambour is very small, the membrane is made of thick rubber, and the whole, including the tube that connects it to the heart, is filled with a strong saline solution (saturated solution of sodium sulphate).

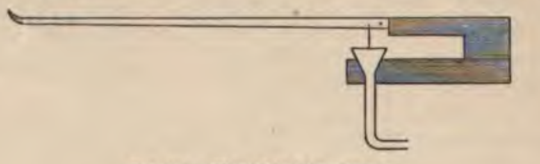

FIG. 251.—Hürthle's Manometer.

The tracing obtained by this instrument, when connected with the interior of the ventricle, is represented in the next figure.

The auricular systole causes a small rise of pressure A B; it lasts about ·05 second. It is immediately followed by the ventricular contraction, which lasts from B to D. From B to C the ventricle is getting up pressure, so that at C it equals the aortic pressure. This takes ·02 to ·04 second. Just beyond C the aortic valves open, and blood is driven into the aorta; the outflow lasts from C to D (·2 second). At D the ventricle relaxes. The flat part of the curve is spoken of as the *systolic plateau,* and according to the state of the heart and the peripheral resistance may present a gradual ascent or descent; it occupies about ·18 second. Almost immediately after the relaxation begins the intraventricular pressure falls below the aortic, so that the aortic valves close near the upper part of the descent at E.

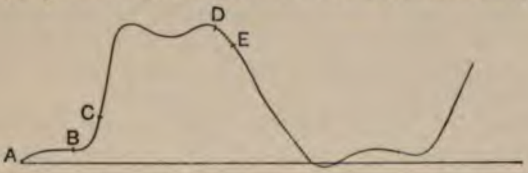

FIG. 252.—Curve of intraventricular pressure. (After Hürthle.)

The amount of pressure in the heart is measured by a manometer, which is connected to the heart by a tube containing a valve. This was first used by Goltz and Gaule. If the valve permits fluid to go only from the heart, the manometer will indicate the maximum pressure ever attained during the cycle. If it is turned the other way, it will indicate the minimum pressure. The following are some of the measurements taken from the dog's heart in terms of millimetres of mercury:—

	Maximum pressure.	Minimum pressure.
Left ventricle	140 mm.	– 30 to 40 mm.
Right ventricle	60 mm.	– 15 mm.
Right auricle	20 mm.	– 7 to 8 mm.

By a negative (–) pressure one means that the mercury is sucked up in the limb of the manometer towards the heart.

Another valuable instrument introduced by Hürthle is called the differential manometer. In this instrument, two cannulæ are brought into connection with tambours (A and B) which work on points of a lever at equal distances from and on opposite sides of its fulcrum (F). The lever sets in motion a writing style (S). This instrument enables us to determine the relations of the pressure changes in any two cavities. For instance, suppose A is connected to the left ventricle, and B to the aorta; when the pressure in the ventricle is greater than that in the aorta, the writing style will be raised; when the pressure in the aorta is greater than that in the ventricle, the style will fall; when the two pressures are equal, it will be in the zero position.

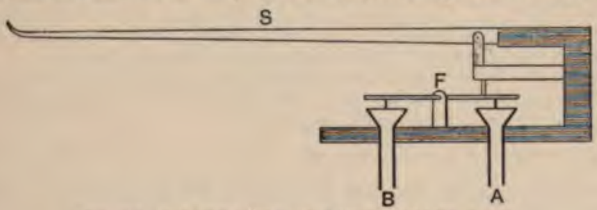

FIG. 253.—Diagram of Hürthle's differential Manometer.

Frequency of the Heart's Action.

The heart of a healthy adult man contracts about 72 times in a minute; but many circumstances cause this rate, which of course corresponds with that of the arterial pulse, to vary even in health. The chief are age, temperament, sex, food and drink, exercise, time of day, posture, atmospheric pressure, temperature. Some figures in reference to the influence of age are appended.

The frequency of the heart's action gradually diminishes from the commencement to near the end of life, but is said to rise again somewhat in extreme old age, thus:—

Before birth the average number of pulsations per minute is	150
Just after birth	from 140 to 130
During the first year	,, 130 to 115
During the second year	,, 115 to 100
During the third year	,, 100 to 90
About the seventh year	from 90 to 85
About the fourteenth year	,, 85 to 80
In adult age	,, 80 to 70
In old age	,, 70 to 60
In decrepitude	,, 75 to 65

In health there is observed a nearly uniform relation between the frequency of the beats of the heart and of the respirations; the proportion being, on an average, 1 respiration to 3 or 4 beats. The same relation is generally maintained in the cases in which the action of the heart is naturally accelerated, as after food or exercise; but in disease this relation may cease.

Work of the Heart.

Waller compares the work performed by the heart in the day to that done by an able-bodied labourer working hard for two hours. The heart's work consists in discharging blood against pressure, and in imparting velocity to it. Thus, if V represents the output of the heart per beat measured in cubic centimetres, and P the mean pressure in the aorta, m the mass of the blood, and v the velocity imparted to it; the work W is given by the equation:—

$$\begin{aligned} W &= VP + \tfrac{1}{2}mv^2 \\ &= Vgdh + \tfrac{1}{2}mv^2 \end{aligned}$$

where h is the mean pressure in the aorta expressed in centimetres of blood, d the density of the blood, and g the acceleration of gravity (981).

If now a is the transverse section of the aortic orifice, b that of the aorta, t the duration of the ventricular systole, and t_1 the duration of the cardiac cycle, then, if v_1 is the mean velocity of the blood in the aorta,

$$V = avt = bv_1t_1.$$

Let us assume that the output of the heart is 110 c.c. per beat. The duration of the cardiac cycle is 0·8 sec., and that of the ventricular systole is 0·3 sec. The diameter of the aorta is about 3 cms. and that of the aortic orifice 2·6 cms. Remembering that the radius in each case is half the diameter, we have:—

$$110 = \pi(1{\cdot}3)^2 \times 0{\cdot}3 \times v = \pi(1{\cdot}5)^2 \times 0{\cdot}8 \times v_1$$

Therefore $v = 86{\cdot}03$, and $v_1 = 19{\cdot}45$ cms. per second.

That is, the velocity of the blood as it is discharged from the heart is about 4·5 times greater than the mean velocity of the blood in the aorta.

If H represents the mean intraventricular pressure during the time blood is being discharged into the aorta, measured in cms. of blood, and h the mean aortic pressure over the same time, then :—

$$v^2 = 2g(H-h).$$

Or
$$\begin{aligned} H &= h + \frac{v^2}{2g} \\ &= h + \frac{(86{\cdot}03)^2}{2 \times 981} \\ &= h + 3{\cdot}77 \text{ cms. of blood.} \end{aligned}$$

That is, the mean intraventricular pressure during the time the semilunar valves are open is only 3·77 cms. of blood or 0·28 cms. of mercury higher than the mean aortic pressure during the same time. We may take the mean aortic pressure during the duration of systole as approximately 12 cms. of mercury or 156 cms. of blood, if we take the density of mercury as being 13 times that of the blood.

Now if E_ρ represents the total potential energy created by the heart per beat, then,

$$E_\rho = VgdH.$$

A part of this energy, E_κ, is converted into kinetic energy since velocity is imparted to the blood. This amount is given by the formula :—

$$E_\kappa = \tfrac{1}{2} Vdv^2.$$

From these two formulæ

$$E_\rho = 110 \times g \times 1{\cdot}05 \times (156 + 3{\cdot}77) \text{ ergs}$$

or
$$\begin{aligned} &= 110 \times 1{\cdot}05 \times (159{\cdot}77) \text{ grm. cms.} \\ &= 18453{\cdot}4 \text{ grm. cms.} \end{aligned}$$

Again
$$\begin{aligned} \frac{E_\rho}{E_\kappa} &= \frac{VgdH}{\frac{1}{2}\, Vdv^2} \\ &= \frac{2gH}{v^2}. \\ &= \frac{H}{H-h} \\ &= \frac{159{\cdot}77}{3{\cdot}77} \\ &= 40 \text{ approximately.} \end{aligned}$$

That is, $\frac{1}{40}$ of the total energy of the heart's beat is used in imparting velocity to the blood.

When the blood reaches the aorta its velocity is gradually checked, *i.e.*, some of the kinetic energy imparted to it by the heart is reconverted into energy of pressure. The remaining kinetic energy is given by the equation :—

$$\begin{aligned} E_\kappa^1 &= \tfrac{1}{2}\, mv_1^{\,2} \\ &= \frac{Vdv_1^{\,2}}{2g} \\ &= 22{\cdot}275 \text{ grm. cms.} \end{aligned}$$

Hence, the kinetic energy of the blood in the aorta is only approximately $\frac{1}{800}$ of the total energy imparted to the blood by the heart.

The Output of the Heart.—The first estimations of the work of the heart, made by Volkmann and Vierordt, gave numbers nearly double those stated in the preceding paragraph. Recent research has shown that their estimate of the output of the heart was excessive. Direct measurements of the heart's output have been made by Stolnikow and Tigerstedt. The former cut off by ligature the whole of the systemic circulation in the dog, and then measured the amount of blood passing through the simplified circulation which consisted only of the pulmonary and coronary vessels by means of a graduated cylinder interposed on the course of the vessels (see fig. 254). Tigerstedt made his observations by means of a Stromuhr (see next chapter) inserted into the aorta. Severe operative measures of this kind, however, interfere with the circulation a good deal.

Gréhant and Quinquand, and Zuntz adopted an indirect method based on the comparison of the amount of oxygen absorbed in the lungs with the amount added to the blood in its passage through the pulmonary circulation.

G. N. Stewart has introduced an ingenious method, the principle of which is the following:—A solution of an innocuous substance, which can be easily recognised and estimated, is allowed to flow for a definite time and at a uniform rate into the heart; the substance selected was sodium chloride. This mingles with the blood and passes into the circulation. At a convenient point of the vascular system, a sample of blood is drawn off just before the injection, and an equal amount during the passage of the salt; the quantity of the sodium chloride solution which must be added to the first sample in order that it may contain as much as the second sample is determined. This determination gives the extent to which the salt solution has been mixed with the blood in the heart, and knowing the quantity of the solution which has run into the heart, the output in a given time can be calculated.

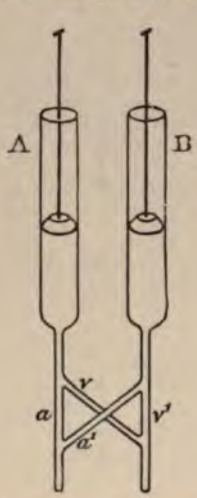

FIG. 254.—Stolnikow's apparatus. A and B are two cylinders fitted with floats provided with writing-points at their upper ends. The tube from the lower end of each bifurcates into two, a and v from A; a' and v' from B. a and a, are united together and enter the right carotid artery; v and v' unite and are inserted into the superior vena cava. The remaining branches of the aorta and the inferior vena cava are tied. B is first filled with defibrinated blood, which passes down v' into the right auricle, thence to the right ventricle, lungs (where it is oxygenated), and then enters the left side of the heart; the left ventricle expels it by the tube a into A, so that the float in A rises while that in B falls. As soon as B is empty the tubes v and a' which were previously clamped are released, and v' and a are clamped instead. The left ventricle now expels its blood by the tube a' into the cylinder B; simultaneously A empties itself through v into the right side of the heart. Zigzag lines are thus traced by the writing-points on the top of the floats, and their frequency enables one to estimate the output of the left ventricle in a given time. (After Starling.)

All these experiments have been on animals. The results obtained necessarily vary with the size of the animal used, and with the rate at which the heart is beating. If the same relationship holds for man as for animals, Stewart calculates that in a man weighing 70 kilos. the output of each ventricle per second is less than 0·002 of the body weight, *i.e.*, about 105 grammes of blood per second, or 87 grammes (about 80 c.c.) per heart beat with a pulse rate of 72. Zuntz obtained rather smaller numbers by his method.

An instrument called the *cardiometer* was invented by Roy for registering the output of the heart. His instrument was made of metal, and oil was used as the transmitting medium in its interior. A simple modification of this applicable to the heart of a small mammal like a cat has been devised by Barnard. It consists of an indiarubber tennis ball with a circular orifice cut in one side of it large enough to admit the heart; a glass tube is securely fixed into a small opening on the opposite side of the ball. The animal is anæsthetised, and its thorax opened. The animal is kept alive by artificial respiration. The pericardium is then opened by a crucial incision, the heart is slipped into the ball; the pericardium overlaps the outside of the ball, and the apparatus is rendered air-tight by smearing the edges of the hole with vaseline. The four corners of the pericardium are then tightly tied by ligatures round the glass tube just mentioned. This tube is connected by a stout indiarubber tube to a Marey's tambour or a piston-recorder, the writing-point of which is applied to a moving blackened cylinder. When the heart contracts, air will be withdrawn from the tambour to the cardiometer; when the heart expands, the air will move in the reverse direction. These movements are written by the end of the lever of the tambour, and variations in the excursions of this lever correspond with variations in the amount of blood expelled from or drawn into the heart with systole and diastole respectively. By calibrating the instrument the actual volume of the blood expelled can be ascertained.

Innervation of the Heart.

The nerves of the heart, which under normal circumstances control its movements, are:—

1. Cardiac branches of the vagus (inhibitory fibres).
2. Cardiac branches of the sympathetic (augmentor and accelerator fibres).

These pass to the heart and terminate in certain collections of ganglion cells in its wall; from these cells fresh fibres are distributed among the muscular fibres. In addition to these nerves, which are efferent, we have to mention:—

3. The sensory or afferent nerves of the heart, the best known of which is called the *depressor* nerve. This nerve, starting from the cardiac tissue, joins the vagus trunk; it passes to the bulb, especially to the vaso-motor centre. We shall therefore postpone its study until we are considering the vaso-motor nerves.

The Vagus.—The ninth, tenth, and eleventh cranial nerves arise close together from the grey matter in the floor of the fourth ventricle, and leave the bulb by a number of rootlets. These rootlets are divided by Grossmann into three groups, *a*, *b*, and *c*; there is a good deal of blending of the rootlets before they ultimately emerge from the skull, but the *a* group corresponds fairly well with the fibres of the glossopharyngeal, *b* with those of the vagus, and *c* with those of the spinal accessory. The rootlets of the tenth nerve pass through two ganglia called respectively the *jugular ganglion*, and the *ganglion trunci vagi*. The fibres of the spinal accessory nerve which join the vagus are chiefly motor, especially to the larynx, but some go to the heart. The vagus gives off branches to many organs, pharynx, larynx, heart, lungs, œsophagus, and various abdominal organs. We have, however, in this place only to deal with its cardiac fibres. It has been known since the experiments of the Brothers Weber in 1845 that stimulation of one or both vagi produces slowing or stoppage of the beats of the heart. It has since been shown that in all vertebrate animals, this is the normal result of vagus stimulation; the phenomenon is called *inhibition*, and the nerve-fibres *cardio-inhibitory*. Section of one vagus produces slight acceleration of the heart; this result is better marked when both vagi are divided. This shows that the restraining influence of the vagus is being continuously exercised; it is, however, found that the amount of vagus control so exercised varies a good deal in different animals. The most potent artificial stimulus which can be applied to the vagus nerve to produce inhibition of the heart is a rapidly interrupted induction current; severe mechanical stimuli have a slight effect, but chemical and thermal stimuli are ineffective.

A certain amount of confusion has arisen as to the effect of vagus stimulation, because so many experiments have been made on the frog. In this animal the sympathetic fibres join the vagus after it leaves the skull, and so what is usually called the vagus in this animal should more properly be termed the *vago-sympathetic*. It will readily be understood that by stimulating a mixed nerve, one obtains an intermixture of effects. If, however, one stimulates the intracranial vagus before the sympathetic blends with it, a pure inhibitory effect is obtained. Figs. 255 and 256 show the common effect of stimulating the mixed trunk; the inhibitory effect is usually manifested first, and this is followed by the augmentor effect due to sympathetic action. But it is by no means infrequent to obtain the opposite result. It is often stated that the right nerve contains more

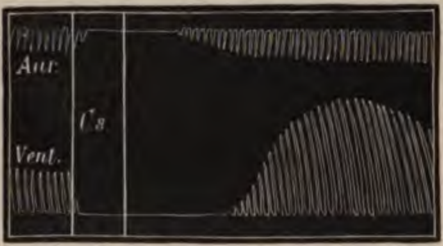

FIG. 255.—Tracing showing the actions of the vagus on the heart. *Aur.*, auricular; *Vent.*, ventricular tracing. The part between the perpendicular lines indicates the period of vagus stimulation. *C.*8 indicates that the secondary coil was 8 *c.m.* from the primary. The part of the tracing to the left shows the regular contractions of moderate height before stimulation. During stimulation, and for some time after, the beats of auricle and ventricle are arrested. After they commence again they are small at first, but soon acquire a much greater amplitude than before the application of the stimulus. (From Brunton, after Gaskell.)

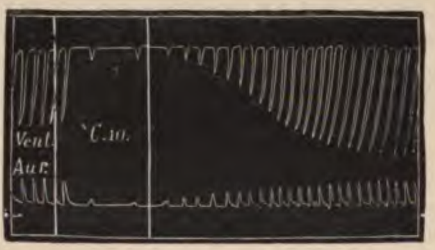

FIG. 256.—Tracing showing diminished amplitude and slowing of the pulsations of the auricle and ventricle without complete stoppage during stimulation of the vagus. (From Brunton, after Gaskell.)

inhibitory fibres than the left, but this is by no means a constant rule. One can always obtain good inhibition if the stimulus is applied to the wall of the sinus; here one stimulates the post-ganglionic fibres which originate from the nerve-cells in the sinus ganglion around which the vagi terminate.

The effect of the stimulus is not immediately seen; one or more beats may occur before stoppage of the heart takes place, and slight stimulation may produce only slowing and not complete stoppage of the heart (fig. 256). The stoppage may be due either to prolongation of the diastole, as is usually the case, or to diminution of the systole. Vagus stimulation lessens the conductivity of the cardiac tissue, but it does not abolish the irritability of the heart-muscle, since mechanical stimulation may bring out a beat during the stand-still caused by vagus stimulation. The inhibition of the beats varies in duration, but if the stimulation is a prolonged one, the beats reappear before the current is shut off. This is known as "vagus escape," and occurs in all animals; it is probably due to fatigue of the vagal endings.

The Sympathetic.—The influence of the sympathetic is the reverse of that of the vagus. Stimulation of the sympathetic produces acceleration of the heart-beats, and according to most observers, section of the nerve produces no slowing. Hence the nerve is not in constant action like the vagus. The acceleration produced by stimulation of the sympathetic fibres is accompanied by increased force, and so the action of the nerve is also termed *augmentor*. It is probable that the augmentor fibres are distinct from the accelerator fibres, because in mammals one or two of the small nerves leaving the stellate ganglion on stimulation produce augmentation without acceleration.

The fibres of the sympathetic system which influence the heart-beat in the frog, leave the spinal cord by the anterior root of the third spinal nerve, and pass by the ramus communicans to the third sympathetic ganglion, then to the second sympathetic ganglion, then by the annulus of Vieussens (round the subclavian artery) to the first sympathetic ganglion, and finally in the main trunk of the sympathetic, to near the exit of the vagus from the cranium, where it joins that nerve and runs down to the heart within its sheath, forming the joint vago-sympathetic trunk. These fibres are indicated by the dark line in fig. 257. The fibres of the sympathetic seen running up into the skull are for the supply of blood-vessels there. It should be noted that the frog has no spinal accessory nerve.

In the mammal the sympathetic fibres leave the cord by the second and third dorsal nerves, and possibly by anterior roots of two or more lower nerves; they pass by the rami communicantes to the ganglion stellatum, or first thoracic ganglion, and thence by the annulus of Vieussens to the inferior cervical ganglion of the sympathetic; fibres from the annulus, or from the inferior cervical ganglion, proceed to the heart (see fig. 258).

In man, the cardiac branches of the sympathetic travel to the heart from the annulus of Vieussens and cervical sympathetic in superior, middle, and lower bundles of fibres. These pass into the cardiac plexus, and surrounding the coronary vessels ultimately reach the heart. They probably contain vaso-motor fibres for these vessels, as well as the more important fibres for the heart itself.

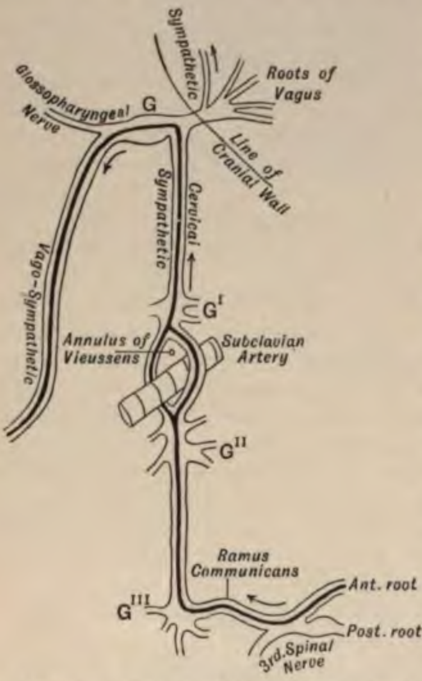

FIG. 257.—Heart nerves of frog. (Diagrammatic.)

By stimulating each rootlet in his three groups, Grossmann found the cardio-inhibitory fibres in the lower two or three rootlets of group *b* and the upper rootlet of group *c*. There are probably differences in different animals. In the cat and dog Cadman finds that the rootlets in the *a* group are respiratory and afferent inhibitory, and that all the efferent inhibitory fibres are in group *c*.

The inhibitory fibres are medullated, and only measure 2μ to 3μ in diameter; they pass to the heart and have their cell-stations in the ganglia of that organ. The sympathetic fibres, on the other hand, reach the heart as non-medullated fibres; they have their cell-stations in the sympathetic (inferior cervical and first thoracic) ganglia. The augmentor and accelerator centres in the central nervous system have not yet been accurately localised.

Influence of Drugs.—The question of the action of drugs on the heart forms a large branch of pharmacology. We shall be content here with mentioning two only, as they are largely used for experimental purposes by physiologists. *Atropine* produces considerable augmentation of the heart-beats by paralysing the inhibitory mechanism. *Muscarine* (obtained from poisonous fungi) produces marked slowing, and in larger doses temporary stoppage of the heart. Its effect is a prolonged inhibition, and can be removed by the action of atropine. The action of atropine cannot, however, be easily antagonised by muscarine; a large dose is necessary. That these drugs act on the nerves, and not the muscular substance of the heart, is shown by the fact that in the hearts of early embryos, so early that no nerves have yet grown to the heart, these drugs have little or no effect. (Pickering.)

Reflex Inhibition.—Thus there is no doubt that the vagi nerves are simply the media of an inhibitory or restraining influence over the action of the heart, which is conveyed through them from the centre in the medulla oblongata, which is always in operation. The restraining influence of the centre in the medulla may be reflexly *increased* by stimulation of many afferent nerves, particularly those from the nasal mucous membrane, the larynx, and the lungs. A blow on the abdomen causes inhibition and fainting; a blow on the larynx, even a moderate one, will kill. There is no comparison between the ease with which stimulation of the laryngeal or pulmonary fibres produces inhibition, as compared to the difficulty of obtaining inhibition from the alimentary tract. Chloroform vapour* and tobacco smoke in some people and animals, by acting on the terminations of the vagi or their branches in the respiratory system, may also produce reflex inhibition of the heart. Some very remarkable facts concerning the readiness by which reflex inhibition of the fish's heart may be produced were made out by M'William; any slight irritation of the tail, gills, mucous membrane of mouth and pharynx, or of the parietal peritoneum, causes the heart to stop beating.

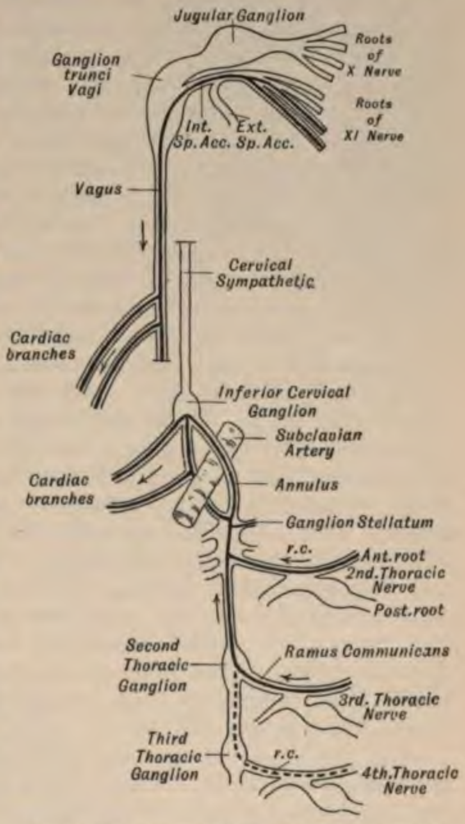

FIG. 258.—Heart nerves of mammal. (Diagrammatic.)

In connection with the subject of reflex inhibition, it may be mentioned in conclusion that though we have no voluntary control over the heart's movements, yet cerebral excitement will produce an effect on the rate of the heart, as in certain emotional conditions.

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* Embley, however, considers that the usual cause of sudden death during the early stages of chloroform narcosis is the direct action of the drug on the vagus centre. In animals, cutting the vagi immediately sets the heart going again.

The Excised Heart.

The heart beats after its removal from the body; in the case of the frog and other cold-blooded animals, this will go on for hours, and under favourable circumstances for days. In the case of the mammal, it is more a question of minutes unless the heart is artificially fed through the coronary artery with arterial blood. If this is done, especially in an atmosphere of oxygen, the dog's heart, or even strips of the dog's heart, can be kept beating for hours. (Porter.) Ringer's salt solution (see p. 256), if well oxygenated, will also keep an excised mammal's heart beating for hours, especially if a little dextrose is added to the solution. (Locke.) At one time the rhythm was supposed to originate from the intrinsic nervous system of the heart; the heart was regarded almost as a complete organism, possessing not only parts capable of movement, but also a nervous system to initiate and regulate those movements.

We now, however, look upon the muscular tissue of the heart, rather than its nerves, as the tissue which possesses the power of rhythmical activity, because muscular tissue which has no nerves at all possesses this property. For instance, the ventricle apex of the frog's or tortoise's heart possesses no nerve-cells, but if it is cut off and fed with a suitable nutritive fluid at considerable pressure, it will beat rhythmically. (Gaskell.) The apparatus by which this may be accomplished we shall study at the end of this chapter. The middle third of the ureter is another instance of muscular tissue free from nerves, but which nevertheless executes peristaltic movements. Perhaps, however, the most striking instance is that of the fœtal heart, which begins to beat directly it is formed, long before any nerves have grown into it.

The power of rhythmical peristalsis therefore resides in the muscular tissue itself, though normally during life it is controlled and regulated by the nerves that supply it.

The intracardiac nerves have been chiefly studied in the frog; the two vago-sympathetic nerves terminate in various groups of ganglion cells; of these the most important are *Remak's ganglion*, situated at the junction of the sinus with the right auricle; and *Bidder's ganglion*, at the junction of the auricles and ventricle. A third collection of ganglion cells (*von Bezold's ganglion*) is situated in the inter-auricular septum. From the ganglion cells, fibres spread out over the walls of the sinus, auricles, and upper part of the ventricle. Remak's ganglion used to be called the local inhibitory centre of the heart; it is really the cell-station of the inhibitory fibres, and stimulation of the heart at the sino-auricular junction is the most certain way of obtaining stoppage of the heart. Bidder's ganglion was called the local accelerator centre for a corresponding reason.

The accompanying figures show the vagal terminations in Remak's ganglion (fig. 259), some isolated nerve-cells from this ganglion (fig. 260); and fig. 261 is a rough diagram to indicate the positions of the two principal ganglia.

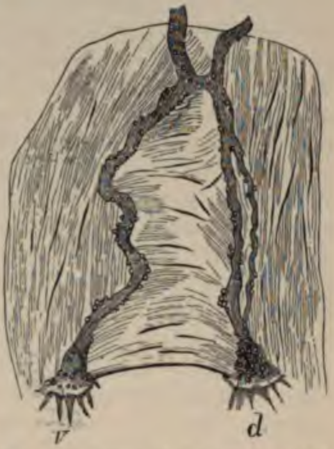

FIG. 259.—Course of the nerves in the auricular partition wall of the heart of a frog. *d*, dorsal branch; *v*, ventral branch. (Ecker.)

Conduction in the Heart.—The question has been discussed whether the wave of contraction is propagated along the heart-wall by nervous or muscular connection. The slow rate of propagation of the wave points to the link being a muscular one, and it will be remembered that histology lends support to this view, the muscular fibres being connected to each other by intercellular bridges of protoplasm (see p. 87). An experimental proof of the same view is the following: if a strip of the heart wall is taken and a number of cuts going nearly completely across it, be made first from one side, then from the other, all the nerves must be cut through at least once, and the only remaining tissue not severed is muscular, yet the strip still continues to beat; in other words, the propagation is *myodromic.* The passage of the wave from one chamber to another is also myodromic. The slow rate of propagation indicates that this is so, and the view has been fully proved by the discovery of muscular fibres passing across from one chamber to the next.

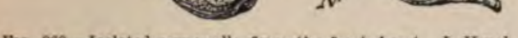

FIG. 260.—Isolated nerve-cells from the frog's heart. I. Usual form. II. Twin cell. *C*, capsule; *N*, nucleus; *N'*, nucleolus; *P*, process. (From Ecker.)

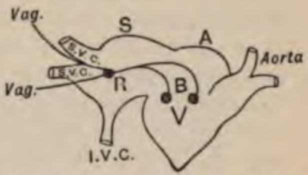

FIG. 261.—Diagram of ganglia in frog's heart. R. Remak's, B, Bidder's ganglion; S, sinus; A, right auricle; V, ventricle.

Blocking.—This phenomenon has been chiefly studied by Gaskell. It appears that under normal conditions the wave of contraction in the heart starts at the sinus, and travels over the auricles to the ventricle; the irritability of the muscle and the power of rhythmic contractility is greatest in the sinus, less in the auricles, and still less in the ventricles. Under ordinary conditions the apical portion of the ventricles exhibits very slight power of spontaneous contraction. The importance of the sinus as the starting-point of the peristalsis can be shown by warming it. If a frog's heart is warmed by bathing it in warm salt solution at about body temperature, it beats faster; this is due to the sinus starting a larger number of peristaltic waves; that this is the case may be demonstrated by warming localised portions of the heart by a small galvano-cautery; if the sinus is warmed the heart beats faster, but if the auricles or ventricles are warmed there is no alteration in the heart's rate. The sinus in the frog's heart, and that portion of the right auricle in the mammal's heart which corresponds to the sinus, is always the last portion of the heart to cease beating on death, or after removal from the body (*ultima moriens*, Harvey). This is an additional proof of the superior rhythmical power which it possesses.

But to continue our description of the phenomenon known as blocking; it is supposed that the wave starting at the sinus is more or less blocked by a ring of lower irritability at its junction with the auricle; again, the wave in the auricle is similarly delayed in its passage over to the ventricle by a ring of lesser irritability, and thus the wave of contraction is delayed at its entrance into both auricular and ventricular tissue. By an arrangement of ligatures, or, better, of clamps, one part of the heart may be isolated from the other portions, and the contraction when aroused by an induction shock may be made to stop in the portion of the heart muscle in which it begins. It is not unlikely that the contraction of one portion of the heart acts as a stimulus to the next portion, and that clamps and ligatures prevent this normal propagation of stimuli. It must not, however, be thought that the wave of contraction is incapable of passing over the heart in any other direction than from the sinus onwards; for it has been shown that by the application of appropriate stimuli at appropriate instants, the natural sequence of beats may be reversed, and the contraction starting at the arterial part of the ventricle may pass to the auricles and then to the sinus.

If Gaskell's clamps or ligatures are not applied sufficiently tight one often sees partial blocking, a few waves get through but not all; in the experiment described on the preceding page, in which the heart wall is left connected with other parts by a small portion of undivided muscular tissue, the effect is much the same, the wave is only able to pass the block every second or third beat.

The Stannius Experiment.—This consists in applying a tight ligature to the heart between the sinus and the right auricle; the sinus continues to beat, but the rest of the heart is quiescent. The quiescent parts of the heart may be made to contract in response to mechanical or electrical stimulation. If a second ligature is applied to the junction of the auricles with the ventricle, the ventricle begins to beat again; the auricles may also beat, but they usually do not. According to Gaskell, the effect of the first ligature is simply an example of blocking; it is, however, difficult to wholly accept this view, for if instead of applying a ligature at the sino-auricular junction, the heart wall is simply cut through at this spot, the auricles and ventricle are not thereby always rendered quiescent. It appears probable, therefore, that there is some truth in the older view that the ligature acts as a stimulus irritating the vagal terminations in Remak's ganglion, and so eliciting a condition of prolonged inhibition; this, however, passes off after a variable time, and the auricles and ventricle once more beat rhythmically. It is impossible to explain the effect of the second Stannius ligature except on the hypothesis that it acts as a stimulus, and there is no *à priori* reason why the two ligatures should act in opposite ways.

The fact that the Stannius heart is quiescent has enabled physiologists to study the effects of stimuli upon heart muscle. A single stimulus produces a single contraction, which has a long latent period, is slow, and propagated as a wave over the heart at the rate of $\frac{2}{5}$ to $\frac{3}{5}$ inch, or 10—15 mm. a second. A second stimulus causes a rather larger contraction, a third one larger still, and so on for some four or five beats, when the size of the contraction becomes constant. This *staircase* phenomenon, as it is called, is also seen in voluntary muscle (see p. 117), but it is more marked in the heart. The following tracing shows the result of an actual experiment:—

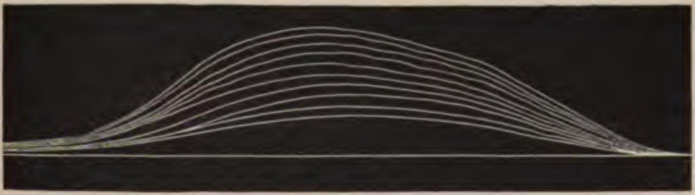

FIG. 262.—Staircase from frog's heart. This was obtained from a Stannius preparation; an induction shock being sent into it with every revolution of the cylinder (rapid rate). The contractions became larger with every beat. To be read from right to left.

There are, however, more marked differences than this between voluntary and heart muscle. The first of these is, that the amount of contraction does not vary with the strength of the stimulation. A stimulus strong enough to produce a contraction at all brings out as big a beat as the strongest. The second is, that the heart muscle has a long *refractory* period; that is to say, after the application of a stimulus, a second stimulus will not cause a second contraction until after the lapse of a certain interval called the *refractory period.* The refractory period lasts as long as the contraction period. The third difference depends on the second, and consists in the fact that the heart muscle can never be thrown into complete tetanus by a rapid series of stimulations; with a strong current there is a partial fusion of the beats, but this is entirely independent of the rate of faradisation. Indeed, as a rule, the heart responds by fewer beats to a rapid than to a slow rate of stimulation.

In spite of these differences there are many and important resemblances between heart muscle and voluntary muscle.

The thermal and chemical changes are similar; there is a using-up of oxygen and a production of carbonic acid and sarco-lactic acid. The using-up of oxygen was well illustrated by an experiment of Yeo's. He passed a weak solution of oxy-hæmoglobin through an excised beating frog's heart, and found that after it had passed through the heart, the solution became less oxygenated and venous in colour.

The electrical changes are also similar, and have already been dwelt upon in Chapters XII. and XIV.

Instruments for Studying the Excised Heart.

If a frog's heart is simply excised and allowed to remain without being fed, it ceases to beat after a time varying from a few minutes to an hour or so; but if it is fed with a nutritive fluid, it will continue to beat for many hours. A very good nutritive fluid is defibrinated blood diluted with twice its volume of physiological saline solution. Ringer has, however, shown that nearly as good results are obtained with physiological saline solution to which minute quantities of calcium and potassium salts have been added; in other words, the inorganic salts of the blood will maintain cardiac activity for a time without the addition of any organic material. Howell has shown that such an inorganic mixture is especially efficacious in throwing the sinus or venous end of the heart into rhythmical action. The normal stimulus for the starting of the heart-beat is therefore to be sought in the mineral constituents of the blood. These mineral constituents in solutions are broken up into their constituent ions; and of these the sodium ions are the most potent in producing rhythmical activity. (Loeb.)

The fluid is passed through the heart by means of a perfusion cannula (fig. 263). The heart is tied on to the end of the cannula;

the fluid enters by one and leaves by the other tube. Numerous instruments have been devised for obtaining graphic records of the heart's movements under these circumstances, but we shall be content with describing a few of the best. They have been much used in the investigation of the effects of drugs on the heart, and the results obtained have been of much service to physicians.

(1) The heart having been securely tied on to the perfusion cannula, the circulating fluid is passed through it. One stem of the cannula is then attached by the small side branch on the left in fig. 263 by a tube containing salt solution to a small mercurial manometer, provided with a float, on the top of which is a writing style. The apparatus is arranged so that the movements of the mercury can be recorded by the float and the writing style on a slowly revolving drum. The movements of the mercury are due to changes in the intracardiac pressure.

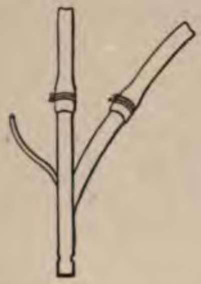

FIG. 263.—Kronecker's Perfusion Cannula, for supplying fluids to the interior of the frog's heart.

It consists of a double tube, one outside the other. The inner tube branches out to the right; thus, when the ventricle is tied to the outer tube of the cannula, a current of liquid can be made to pass into the heart by one tube and out through the other.

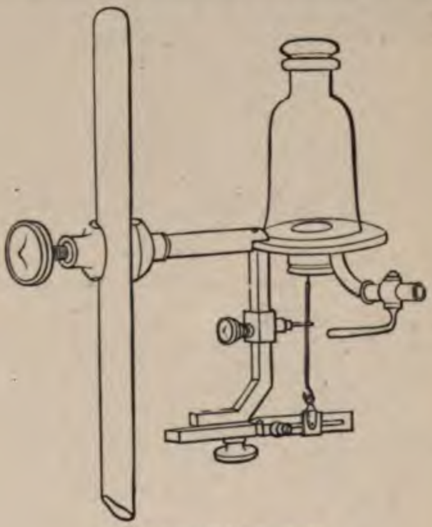

FIG. 264.—Roy's Tonometer.

(2) *Roy's Tonometer* (fig. 264): A small bell-jar, open above, but provided with a firmly fitting stopper, in which is fixed a double cannula, is adjustable by a smoothly ground base upon a circular brass plate, about 2 to 3 inches in diameter. The junction is made complete by greasing the base with lard. In the plate, which is fixed to a stand adjustable on an upright, are two holes, one in the centre, a large one about one-third of an inch in diameter, to which is fixed below a brass grooved collar, about half an inch deep; the other hole is the opening into a pipe provided with a stop-cock. The opening provided with the collar is closed at the lower part with a membrane, which is closely tied by means of a ligature around the groove at the lower edge of the collar. To this membrane a piece of cork is fastened by sealing-wax, from which passes a wire, which is attached to a lever (cut short in the diagram) fixed on a stage below the apparatus.

When using the apparatus, the bell-jar is filled with olive-oil. The heart of a large frog is prepared and the cannula fixed in the stopper is firmly tied into it; the tubes of the cannula communicate with the reservoir of circulating fluid on the one hand, and with a vessel to receive it after it has run through the heart on the other. The cannula with heart attached is passed into the oil, and the stopper firmly secured. Every time the heart enlarges, the membrane is pressed down; every time the heart contracts the membrane is pulled up; the lever follows and magnifies these movements. The lever is adjusted to a convenient elevation and allowed to write on a moving drum. After a short time the heart may stop beating; but two wires are arranged, the one in the cannula, the other projecting from the plate in such a way that the heart can be moved against them by shifting the position of the bell-jar a little. The wires act as electrodes, and can be made to communicate with an induction apparatus, so that induction shocks can be sent into the heart to produce contractions. After a time the heart ceases to beat altogether; and before doing so it becomes irregular. A frequent form of irregularity seen consists of groups of contractions each showing a staircase, separated by long intervals of quiescence (Luciani's Groups).

(3) *Schäfer's Heart-plethysmograph.*—The principle of this apparatus is the same as Roy's. A diagrammatic sketch of it is given in fig. 265. The heart, tied on to a double cannula, is inserted into an air-tight vessel containing oil. On one side of the vessel is a tube, in which a lightly moving piston is fitted; to this a writing-point is attached. The piston is moved backwards and forwards by the changes of volume in the heart causing the oil to alternately recede from and pass into this side tube. The corresponding tube on the other side can be opened and the tube with the piston closed when one wishes to cease recording the movements.

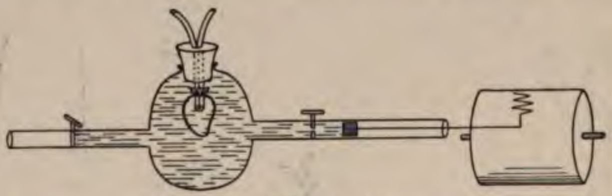

FIG. 265.—Schäfer's Heart-plethysmograph.

(4) In order to obtain a beating heart after excising it from a mammal, the following procedure should be adopted. A rabbit is killed by bleeding or pithing; the heart enclosed in the pericardium is then quickly cut out, and gently kneaded to free it from blood, in some warm Ringer's solution. The pericardium is then dissected off, and a cannula tied into the aorta; this is connected to a burette which is kept full of Ringer's solution. The Ringer's solution must be maintained at body temperature, by a warm water jacket, and must be well oxygenated by letting oxygen bubble through it. The fluid is then allowed to flow, and it enters the coronary arteries, and escapes from the right auricle, which should be freely opened. Under these circumstances the heart will continue to beat for many hours, especially if a little dextrose is added to the circulating fluid. A graphic record may be obtained by putting a small hook into the apex, and attaching this by a thread to a recording lever beneath it. A very good illustration of the usefulness of the method for demonstrating the action of drugs consists in adding a small amount of chloroform to the circulating fluid, and one notices its immediate depressant effect; on the other hand, a minute dose of adrenaline markedly increases the rate and force of the heart.

CHAPTER XXI

THE CIRCULATION IN THE BLOOD-VESSELS

THE movement of the blood from the heart through the arteries, capillaries, and veins back to the heart again, depends on a number of physical factors; and in the consideration of this important subject we shall have to take into account the general laws which regulate the movement of fluids in tubes, as well as their special application to the flow of the blood in the blood-vessels.

The contraction of the heart is the primary propelling force, and the increase of pressure which is thus communicated to the blood it contains causes that blood to enter the arteries; the arterial blood pressure is higher than that in the capillaries, and the capillary pressure is higher than that in the veins; the venous pressure gradually falls as we approach the heart; it is lowest of all in the heart cavities during diastole; fluid moves in the direction of lower pressure, hence the flow of blood is from the heart through the vessels back to the heart again.

The vessels are not rigid tubes, but possess marked elasticity; it is owing to this that the intermittent force of the heart is modified in such a way that the stream of blood in the capillaries is a constant one, and under normal circumstances exhibits no pulsation; the *pulse* is one of the main characters of the arterial flow. A further complication is due to the fact that the vessels through which the blood flows are of varying calibre, and this is the main factor in determining its velocity. Every time an artery divides, the united sectional area of its branches is greater than that of the parent artery, although, of course, each of the individual branches is of smaller calibre. The total bed of the stream is thus becoming greater, until when we reach the capillaries the bed is increased suddenly and enormously, being several hundred times greater than that of the aorta from which they all ultimately spring. In the case of the veins the same is true in the reverse direction; the sectional area of a vein is less than that of the total sectional area of its tributaries; hence as we approach the heart the total bed of the stream is becoming continually smaller, but never so small as in the corresponding arteries; a vein is always twice the size, often more than twice the size of the corresponding artery. Velocity of flow varies inversely with the bed of the stream, the velocity is therefore greatest in the aorta, slows down in the small arteries, and becomes slowest of all in the capillaries where the total bed is widest; we may compare the combined capillaries to a vast lake into which the arterial river flows. On leaving the capillaries, the blood, in traversing the veins once more, becomes accelerated because the bed of the stream becomes narrower, but its speed in a vein is only about half that in the corresponding artery because the bed is twice as great.

In connection with the variation in the bed of the stream we must also consider the question of resistance. If the increase in sectional area took place without division of the stream into numerous branches, the main effect would be to lower resistance to the flow of fluid; but the friction-lowering effect of increased area is much more than counterbalanced by the increased surface of the numerous branches, and there is increased friction on this account. The resistance of the capillaries would be large even for a stream of water, and when we consider that the blood is much more viscid than water, we see the effect must be much greater. The resistance to the flow of fluid along a small tube is in inverse proportion to the fourth power of the diameter, *i.e.*, if the diameter of the tube is halved, the resistance is increased sixteen-fold. Between the arteries and the capillaries are the small arteries or *arterioles;* these vessels are always in a state of moderate or tonic constriction; they may roughly be compared to narrow inlets into the wide capillary lake. The main resistance to the passage of blood through the tissues is situated in the arterioles, and not in the capillaries; this is usually spoken of as the *peripheral resistance*, and it is variable by alterations in the calibre of the arterioles, their muscular tissue being under the control of nerves which are termed *vaso-motor*.

The main resistance is in the arterioles and not in the capillaries for the following reason: each individual capillary is small, and its resistance therefore great, but their number is so immense, and the total bed so large that the resultant resistance offered is comparatively small. This is well brought out by a comparison of the velocity in the two cases; in the arterioles the velocity has to be high in order to supply with blood the large capillary areas springing from them; in the capillaries, as we have already seen, the velocity is low.

After this general account of the main features of the circulation, we can now pass to a detailed description of the various points raised.

Use of the Elasticity of the Vessels.

If a pump is connected to a rigid tube, such as a glass tube, filled with water, and a certain amount of water is forced into the tube, an exactly equal amount of water is driven out from the open end. During the intervals of pumping the flow ceases, accurately at the instant the inflow stops. If in the next place the open orifice is constricted and the pumping continued as before, the outflow is still restricted to the time during which water is being driven into the tube. The only difference is that a greater force of pumping will be required if the pump is to empty itself in the same time as before, and the force required will increase in proportion to the degree of constriction of the orifice, until with a fairly considerable constriction the force required will be enormous.

If the rigid tube is replaced by an elastic one with a wide free opening, the outflow will again be intermittent but not quite restricted to the time of the pumping. This latter difference is because the elastic wall of the tube will stretch a little at each output of the pump, and this continues after the pump has ceased to discharge, and will then recover, at the same time driving out the extra small amount of fluid it contained, after the pump has ceased to act. The flow will thus be intermittent, but the outflow will last for a short time longer than the inflow. This persistence will increase with the resistance of the tube, with the velocity of the inflow, and lastly with the mass of the column of fluid lying in the tube. If now the orifice be diminished, the duration of the outflow will begin to increase still further, and, as the constriction is increased more and more, will gradually extend over the diastolic period of the pumping. The amount of work required to drive the fixed volume of fluid through the constricted orifice is the same with a rigid and with an elastic tube. In the former case, however, the duration of the outflow is of necessity the same as that of the inflow, whereas in the second case this time is prolonged. Consequently the rate of working in the first case must exceed that in the second in proportion to this difference of time, or the maximum pressure set up in the former case is far greater than in the latter. If the constriction of the orifice of the elastic tube is still further increased, a point is at last reached at which the outflow lasts throughout the whole cycle of the pump, and here therefore the energy imparted to the fluid by the pump is converted into a pressure energy represented by the tension of the elastic walls of the tube, and this energy is given out again after the fluid has ceased to enter the tube and is just sufficient to exactly drive out the stored fluid during the resting period. If the constriction be carried still further, the tube will not be able to empty itself during the diastolic period, and when the second inflow begins, some of the fluid will be still distending the tube, *i.e.*, the pressure will not have fallen to zero. With the second inflow the maximum pressure reached will be higher than before, but still the force acting throughout the whole of the cycle may not be sufficient to empty the tube to the extent found at the commencement of that inflow, and we may find a further volume of fluid retained within the tube, and the pressure just before the next inflow still higher than in the preceding instance. This summation will continue, until at last a point is reached at which the mean pressure during a complete cycle will be just sufficient to drive out exactly the same volume of fluid as is sent in at each pumping. When this point is reached, the pressure will simply oscillate about this mean position and the outflow from the tube will therefore be continuous, but not necessarily constant. If we still further constrict the orifice, the result is that the mean pressure will rise still further, and the outflow will be of a less remittent character. The latter because the input of the same volume of fluid into the distended tube will produce less marked fluctuations in the driving pressure, since at the end of diastole the pressure still driving the fluid will be high and not nearly zero, as in the former instance. If the constriction is sufficiently increased, a point will ultimately be reached at which the outflow will become not only continuous but also constant. The degree of constriction necessary to produce this effect will depend upon the distensibility of the elastic tube. The more distensible this is, the earlier will this stage be reached, and the lower will be the mean pressure. This is the condition we find in the circulatory system.

Let us now apply this to the body.

At each beat the left ventricle forces about three ounces of blood into the already full arterial system. The arteries are elastic tubes, and the amount of elastic tissue is greatest in the large arteries. The first effect of the extra three ounces is to distend the aorta still further; the elastic recoil of the walls drives on another portion of blood, which distends the next section of the arterial wall, and this distension is transmitted as a wave along the arteries, but with gradually diminishing force as the total arterial stream becomes larger. This wave constitutes the pulse-wave. Between the strokes of the pump, or, in other words, during the periods of diastole, the arteries drive the blood on and so return to their original size. The flow, therefore, does not cease during the heart's inactivity, so that although the force of the heart is an intermittent one, the flow through the capillaries and the veins beyond is a constant one, all trace of pulsation having disappeared. The peripheral resistance which keeps up the blood-pressure in the arteries, and like the constriction at the end of our india-rubber tube, assists in the conversion of the intermittent into a continuous and constant stream, is to be found in the arterioles or small arteries, just before the blood passes into what we have termed the vast capillary lake. These small arteries with their relative excess of muscular tissue, are in health always in a state of moderate tonic contraction.

The large arteries contain a considerable amount of muscular as well as elastic tissue. This co-operates with the elastic tissue in adapting the calibre of the vessels to the quantity of blood they contain. For the amount of blood in the vessels is never quite constant, and were elastic tissue only present, the pressure exercised by the walls of the containing vessels on the contained blood would be sometimes very small, sometimes too great. The presence of a contractile element, however, provides for a certain uniformity in the amount of pressure exercised. There is no reason to suppose that the muscular coat assists in propelling the onward current of blood, except in virtue of the fact that muscular tissue is elastic, and therefore co-operates in the large arteries with the elastic tissue in keeping up the constant flow in the way already described.

The contractility of the arterial walls fulfils a useful purpose in checking hæmorrhage should a small vessel be cut, as it assists in the closure of the cut end, and this in conjunction with the coagulation of the blood arrests the escape of blood.

Blood-pressure.

The circulation of the blood depends on the existence of different degrees of pressure in different parts of the circulatory system; there is a diminution of pressure from the heart onwards through arteries, capillaries, and veins, back to the heart again.

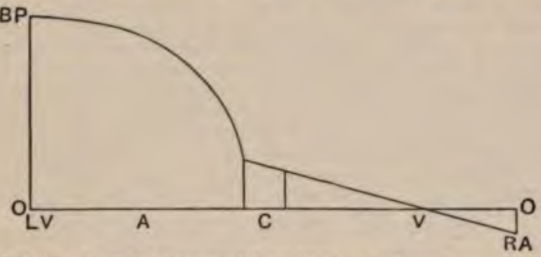

FIG. 266.—Height of blood-pressure (BP) in LV, left ventricle. A, arteries; C, capillaries; V, veins; RA, right auricle; OO, line of no pressure. (After Starling.)

Fig. 266 represents roughly the fall of pressure along the systemic vascular system.

It falls slowly in the great arteries; at the end of the arterial system it falls suddenly and extensively in the course of the arterioles; it again falls gradually through the capillaries and veins till in the large veins near the heart it is negative. Such a diagram of blood-pressure is thus very different from one of velocity; the velocity like the pressure falls from the arteries to the capillaries, but unlike it, rises again in the veins.

We must now study the methods by which blood-pressure is measured and recorded, and the main causes that produce variations in its amount.

In order that we may understand the methods that are used for this purpose, it will be first necessary for us to consider some of the general laws of fluid pressure, and then to study the methods that are employed in an artificial schema of the circulation.

Fluid pressure is a different thing from the pressure of a solid, and is exercised equally in all directions. If a cylindrical vessel, placed vertically, is filled with a cylinder of ice, the pressure of the ice will be exercised on the bottom of the cylinder, but not on its sides. When the ice melts, the water presses on the sides also, and if a hole is made in the cylinder below the level of the upper surface of the water, the water will flow out of the hole, and the force with which it escapes will be proportional to the depth of the hole beneath the surface. If we take a square centimetre as the unit of area, the actual pressure excited on it is $h \times d \times g$, where h is the height of the free surface above the level where we are measuring the pressure, d its density, and g the acceleration of gravity (981). Suppose a gramme of water to flow out, we may consider that this gramme has fallen through a height or *head* h in centimetres from the free surface to the opening; it comes practically from the top, because it is there that the liquid disappears from inside the vessel. In falling the height h, it gives out hg ergs of work.

The unit of force is called a *dyne;* a moving body is said to possess *momentum:* this is measured by the product of its mass and its velocity; thus the effective quantity of motion of a body may be large on account of its having a large mass (for instance, a heavy waggon rolling down a hill), or large velocity (for instance, a bullet speeding through the air). A force continuously applied to a moving mass produces a continuous increase in its rate of movement; this is termed *acceleration*, and force may be defined as the rate of change of momentum; it can be measured, therefore, by observing the amount of momentum it generates in a measured time, and dividing by that time. If a gramme is taken as the unit of mass, a centimetre as the unit of length, and a second as the unit of time, the unit of force

$$= \frac{\text{momentum}}{\text{Time.}} = \frac{\text{gramme-centimetre per second}}{\text{Time in seconds.}}$$

$$= \text{gramme-centimetre per second, per second} = 1 \text{ dyne.}$$

The unit which corresponds to the dyne in the measurement of work is called an *erg*, that is, the work done in lifting a gramme weight through the height of one centimetre; the weight of a gramme is 981 dynes, and the work done in lifting it one centimetre is 981 ergs.

The kinetic energy of a body moving with velocity v is $\frac{1}{2} \times \text{mass} \times v^2$, or for one gramme $\frac{1}{2}v^2$; hence if all the work that liquid can do is spent in giving kinetic energy to it, the velocity with which it will flow out is given by putting the kinetic energy = work done. In other terms:—

$$\tfrac{1}{2}v^2 = gh\text{; hence } v = \sqrt{2gh} \text{ or } h = \frac{v^2}{2g}$$

A liquid, however, has not necessarily a free surface, but may be completely enclosed, as is the water in a system of hydraulic pressure mains, or the blood in the circulatory system. The pressure in such a system at any point may be measured by inserting at that point a vertical tube at right angles to the blood-vessel; the blood would rise in it to a point, and would form a free surface a certain distance up this tube; the head h in the above calculation must be reckoned from this free surface downwards. If, instead of using a tube of fine bore for this purpose, we employ a wider tube, say of ten times greater area, the height or head to which the fluid rises will be the same as in the narrow tube, though naturally the actual weight of fluid supported will be ten times greater; but the weight per unit of area is the same in both cases. When, therefore, we measure the pressure of fluid in terms of the *height* of a column of fluid, like mercury, which it will balance, we really mean that the force of the blood is equal to the weight of the mercury it supports *per unit of area*, and this will naturally be proportional to the height of the column.

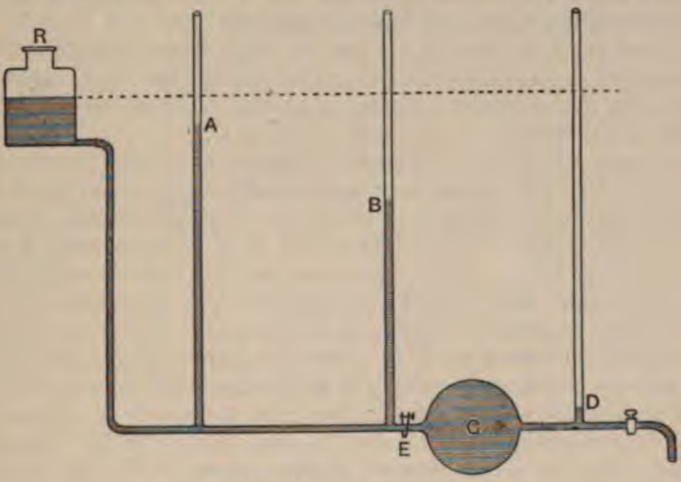

Fig. 267.—Schema to illustrate blood-pressure.

Let us next consider the simple case of a fluid flowing from a reservoir, R (fig. 267), along a tube, which we will imagine is open at the other end.

In the course of the tube we will suppose three upright glass tubes (A, B, and D) are inserted at equal distances. Between B and D there is a bladder, which may be divided into a number of channels by packing it with tow to represent the capillaries, and between B and C, a clip E, which can be tightened or loosened at will, and which will roughly represent the peripheral resistance produced by the arterioles. The far end of the tube is provided with a stop-cock. If this stop-cock is closed there will naturally be no flow of fluid, and the fluid will rise to equal heights indicated by the dotted line in all the upright tubes. This shows that the pressure in all parts of the tube is the same. The upright tubes which measure the lateral pressure exerted by the fluid on the wall of the main tube, are called *pizometers, manometers*, or *pressure measurers.*

If now the stop-cock is opened, the fluid flows on account of the difference of pressure brought about by gravitation; the height of the fluid in the manometers indicates that the pressure is greatest in R, less in A, less still in B, and least of all in D.

On account of the peripheral resistance of the arterioles and capillaries, the pressure is very small in the veins, as indicated by the height of the fluid in the manometer D. The difference between D and B is much more marked than the difference between B and A. If the fluid which flows out of the end of the tube is collected in a jug and poured back into R, we complete the circulation. But the schema is an extremely rough one, and is especially faulty in that the pressure which starts at R is nearly constant and not intermittent. This may be remedied by taking R in the hand, and raising and lowering it alternately. The fluid in the manometers bobs up and down with every rise and fall of R: this is least marked in D. The greater and the faster the movement of R, the greater is the rise of arterial pressure. This is a rough illustration of the fact that increase in the force and frequency of the heart's beat causes a rise of arterial pressure.

Again, if more fluid is poured into R, there is a corresponding rise in fluid in the manometers. This illustrates the rise of pressure produced by an increase in the contents of the vascular system.

And this schema, rough though it is, also serves to illustrate the third important factor in the maintenance of the blood-pressure, namely, the peripheral resistance. This is done by means of the clip E; if the clip is tightened, one imitates increased constriction of the arterioles; if it is loosened, one imitates dilatation of the arterioles. If it is closed entirely, the fluid in A and B rises to the same level as that in R; the pressure of R is not felt at all by C and D, which empty themselves, and the flow ceases. If the clip E is only tightened so as not to be quite closed, the arterial pressure (in A and B) rises, and the venous pressure (in D) falls; if the clip is freely opened, the arterial pressure falls, and the venous pressure rises.

These same facts can be demonstrated by a more perfect circulation schema, such as is represented in fig. 268.

The heart (H) is represented by a Higginson's syringe, which is worked with the hand; the tube from it represents the arterial system, the clip E the resistance of the arterioles; C is the capillary lake, from which the vein (larger than the artery) leads back to the heart H. A and B are two manometers which respectively indicate arterial and venous pressures. Only in place of straight tubes mercurial manometers are used. Each of these is a U-tube about half filled with mercury, and united to the artery or vein by a tube containing fluid. If the mercury in the two limbs of the U is at the same level, the pressure of the fluid in connection with one limb is exactly equal to that exerted by the atmospheric pressure on the other. The mercury, however, is pushed up in the far limb of the manometer connected to the artery, the pressure there being greater than that of the atmosphere; this is therefore called *positive pressure*, and the total amount of pressure is measured by the difference between the levels *a* and *a′*. The manometer B attached to the vein, however, indicates a *negative pressure* (*b b′*), that is a pressure less than that of the atmosphere, so that the mercury in the limb nearest the vein is sucked up.

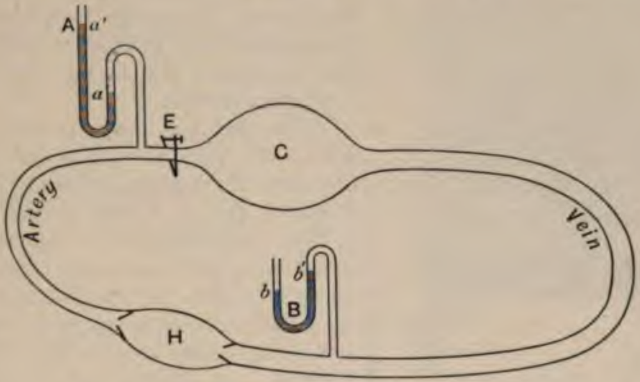

FIG. 268.—Schema of the circulation.

Anderson Stuart's *kymoscope* (fig. 269) is a more complete schema. It consists of a long leaden tube filled with fluid, the two ends of which are connected by an india-rubber tube on which is a valved syringe to represent the heart. On the course of the tube are a large number of open-mouthed upright manometers which indicate the pressure when the syringe is worked, and confer on the tube the elasticity necessary to cause the disappearance of the pulse in the middle region which represents the capillaries. The long leaden tube is twisted round a cylinder, so that the manometers are placed closely side by side.

We can now pass on to the methods adopted in the investigations of blood-pressure in animals.

The fact that the blood exerts considerable pressure on the arterial walls may be readily shown by puncturing any artery; the blood is propelled with great force through the opening, and the jet rises to a considerable height; in the case of a small artery, where the pressure is lower, the jet is not so high as in a large artery: the jerky character of the outflow due to the intermittent action of the heart is also seen. If a vein is similarly injured, the blood is expelled with much less force, and the flow is continuous, not intermittent.

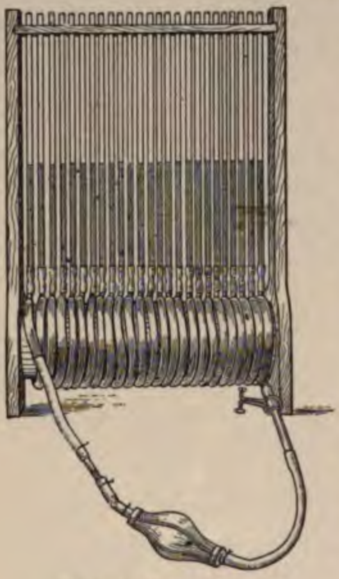

FIG. 269.—Anderson Stuart's Kymoscope.

The first to make an advance on this very rough method of demonstrating blood-pressure was the Rev. Stephen Hales, Vicar of Teddington (1702). He inserted, using a small brass tube as a cannula, a glass tube at right angles to the femoral artery of a horse, and noted the height to which the blood rose in it. This is a method like that which we used in the first schema described (fig. 267). The blood rose to the height of about 8 feet, and having reached its highest point, it oscillated with the heart-beats, each cardiac systole causing a rise, each diastole a fall. Hales also noted a general rise during each inspiration. The method taught Hales these primary truths in connection with arterial pressure, but it possesses many disadvantages; in the first place, the blood in the glass tube very soon clots, and in the second place, a column of liquid eight feet high is an inconvenient one to work with.

The first of these disadvantages was overcome to a great extent by Vierordt, who attached a tube filled with saturated solution of sodium carbonate to the artery, and the blood-pressure was measured by the height of the column of this saline solution which the blood would support.

The second disadvantage was overcome by Poiseuille, who introduced the heavy liquid, mercury, as the substance on which the blood exerted its pressure; and the U-shaped mercurial manometer was connected to the artery by a tube filled with sodium carbonate solution to delay clotting.

The study of blood-pressure cannot, however, be considered to have been in a satisfactory condition until the introduction by Carl Ludwig of the *Kymograph;* that is to say, Poiseuille's *hæmodynamometer* was combined with apparatus for obtaining a graphic record of the oscillations of the mercury. The name *kymograph* or *wave-writer*, we shall see immediately, is a very suitable one.

A skeleton sketch of the apparatus is given in fig. 270.

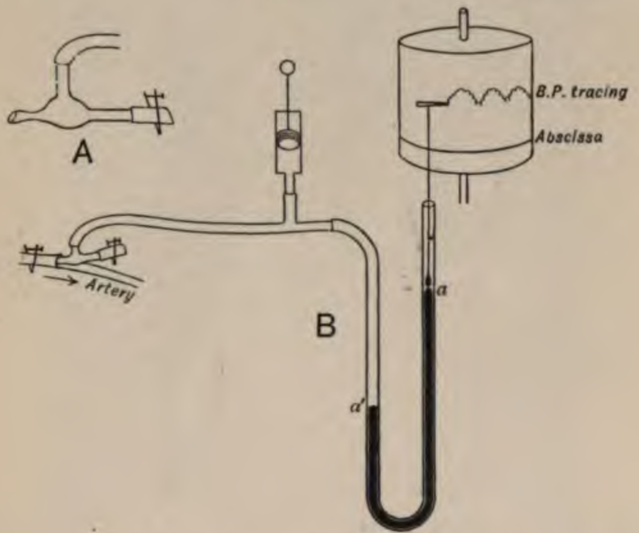

FIG. 270.—Diagram of mercurial Kymograph.

The artery is exposed and clamped, so that no hæmorrhage occurs; it is then opened, and a glass cannula is inserted and firmly tied in. The form of cannula usually employed (François Franck's) is shown on a larger scale at A; the narrow part with the neck in it is tied into the artery towards the heart; the cross piece of the T is united to the manometer; the third limb is provided with a short piece of indiarubber tubing which is kept closed by a clip and only opened on emergencies, such as to clear out a clot with a feather should one form in the cannula during the progress of an experiment.

The tube by means of which the cannula is united to the manometer is not an elastic one, but is made of flexible metal, so that none of the arterial force may be wasted in expanding it. The tube, cannula, and proximal limb of the manometer are all filled with a saturated solution of sodium carbonate, sodium sulphate, or other salt which will mix with blood and delay its clotting. Before the clip is removed from the artery, the pressure is first got up by a syringe (or pressure bottle containing the same saline solution suspended at a good height above the apparatus and connected to it by a tube), so that the mercury rises in the distal limb to a height greater than that of the anticipated blood-pressure; this prevents blood passing into the cannula when the arterial clip is removed.

In the distal limb of the U-tube, floating on the surface of the mercury, is an ivory float, from which a long steel wire extends upwards, and terminates in a writing-point. The writing-point may be a stiff piece of parchment or a bristle which writes on a moving surface covered with smoked paper, or a small brush kept full of ink which writes on a long strip of white paper made to travel by clock-work in front of it. When the two limbs of the mercury are at rest, the writing-point inscribes a base line or abscissa on the travelling surface; when the pressure is got up by the syringe it writes a line at a higher level. When the arterial clip is removed it writes waves as shown in the diagram (fig. 270), the large waves corresponding to respiration (the rise of pressure in most animals accompanying

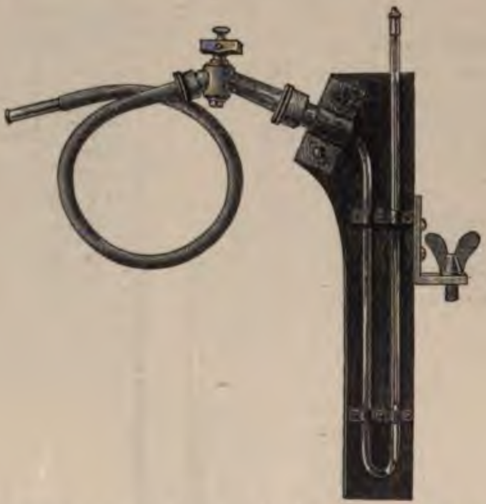

FIG. 271.—The manometer of Ludwig's Kymograph. It is also shown in fig. 272, D, C, E. The mercury which partially fills the tube supports a float in the form of a piston, nearly filling the tube; a wire is fixed to the float, and the writing style or pen fixed to the wire is guided by passing through the brass cap of the tube; the pressure is communicated to the mercury by means of a flexible metal tube filled with fluid.

inspiration),* the smaller ones to the individual heart-beats. The blood-pressure is really twice as great as that indicated by the height of the tracing above the abscissa, because if the manometer is of equal bore throughout, the mercury falls in one limb the same distance that it rises in the other; the true pressure is measured by the difference of level between *a* and *a′* (fig. 270).

Fig. 271 shows a more complete view of the manometer, and fig. 272 is a diagram of the arrangement by means of which it is made into a kymograph.

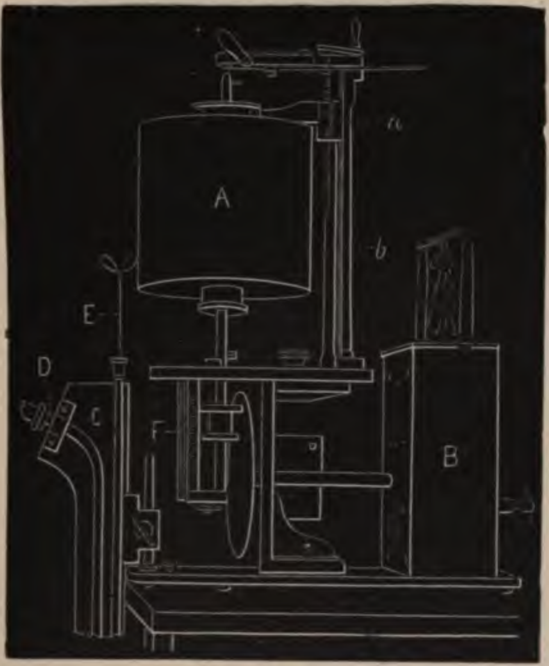

FIG. 272.—Diagram of mercurial Kymograph. A, Revolving cylinder, worked by a clockwork arrangement contained in the box (B), the speed being regulated by a fan above the box; the cylinder is supported by an upright (*b*), and is capable of being raised or lowered by a screw (*a*), by a handle attached to it; D, C, E, represent the mercurial manometer, which is shown on a larger scale in fig. 271.

Fig. 273 shows a typical normal arterial blood-pressure tracing on a larger scale.

In taking a tracing of *venous blood-pressure*, the pressure is so low and corresponds to so few millimetres of mercury, that a saline solution is usually employed instead of mercury. If the vein which is investigated is near the heart, a venous pulse is exhibited on the tracing, with small waves as before corresponding to heart-beats, and larger waves to respiration, only the respiratory rise in pressure now accompanies expiration.

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* The explanation of the respiratory curves on the tracing is postponed till after we have studied Respiration.

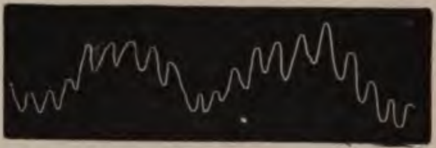

FIG. 273.—Normal tracing, somewhat magnified, of arterial pressure in the rabbit obtained with the mercurial kymograph. The smaller undulations correspond with the heart-beats, the larger curves with the respiratory movements. The abscissa or base line, which on this scale would be several inches below the tracing, is not shown. (Burdon-Sanderson.)

The *capillary pressure* is estimated by the amount of pressure necessary to blanch the skin; this has been done in animals and men (v. Kries, Roy and Brown).

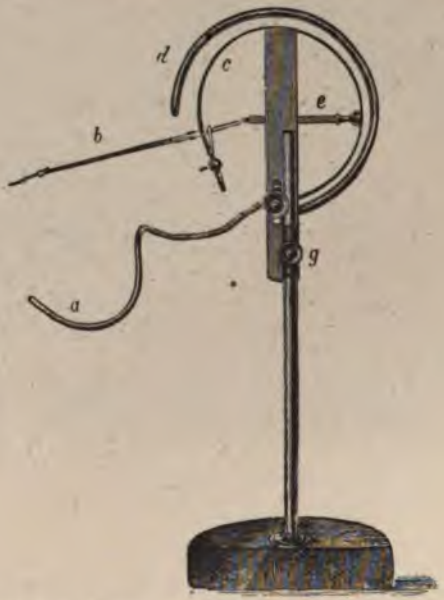

FIG. 274.—A form of Fick's Spring Kymograph. *a*, Tube to be connected with artery; *c*, hollow spring, the movement of which moves *b*, the writing lever; *e*, screw to regulate height of *b*; *d*, outside protective spring; *g*, screw to fix on the upright of the support.

Other manometers are often employed instead of the mercurial one. Fick's is one of these. The blood-vessel is connected as before with the manometer, and the pressure got up by the use of a syringe (which is seen in fig. 275, *g*), before the clip is removed from the artery. The manometer itself is a hollow C-shaped spring filled with liquid; this opens with increase, and closes with decrease of pressure, and the movements of the spring are communicated to a lever provided with a writing-point.

Hürthle's manometer (see p. 242) is also very much used. The advantage of these forms of manometer is that the character and extent of each pressure change is much better seen. In a mercury manometer the inertia is so great that it cannot respond to the very rapid variations in pressure which occur within an artery during each cardiac cycle. If Fick's or Hürthle's manometer is employed, and the surface travels sufficiently fast, these can be recorded (see fig. 276). These instruments, though useful for recording the complete changes in pressure, require calibration: that is, the extent of movement that corresponds to *known* pressures must be ascertained by

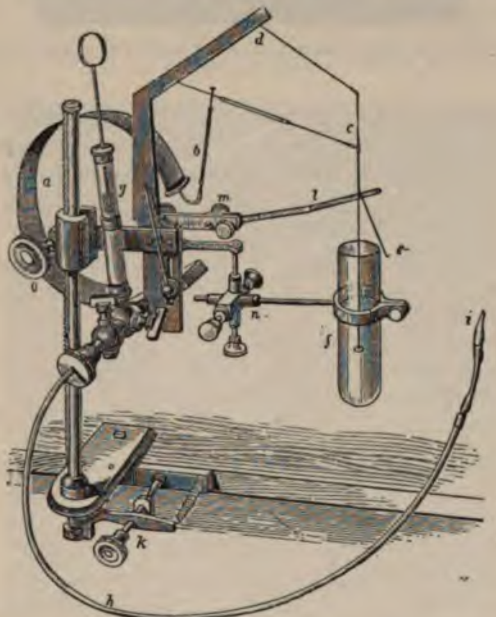

FIG. 275.—Fick's Kymograph, improved by Hering (after M'Kendrick). *a*, Hollow spring filled with alcohol, bearing lever arrangement *b*, *d*, *c*, to which is attached the marker *e*; the rod *e* passes downwards into the tube *f*, containing castor oil, which offers resistance to the oscillations of *e*; *g*, syringe for filling the leaden tube *h* with saturated sulphate of sodium solution, and to apply sufficient pressure as to prevent the blood from passing into the tube *h* at *i*, the cannula inserted into the vessel; *l*, abscissa-marker, which can be applied to the moving surface by turning the screw *m*; *k*, screw for adjusting the whole apparatus to the moving surface; *o*, screw for elevating or depressing the Kymograph by a rack-and-pinion movement; *n*, screw for adjusting the position of the tube *f*.

actual experiment. They teach us that the highest pressure reached during systole may be twice or thrice the lowest attained during diastole.

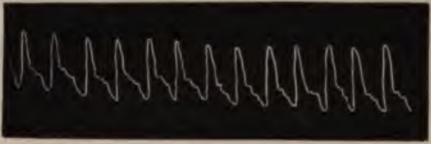

Fig. 276.—Normal arterial tracing obtained with Fick's Kymograph in the dog. (Burdon-Sanderson.)

The following table gives the probable average height of blood-pressure in various parts of the vascular system in man. They have been very largely inferred from experiments on animals:—

Large arteries (*e.g.* carotid) .	+ 140 mm. (about 6 inches) mercury.
Medium arteries (*e.g.* radial) .	+ 110 mm. mercury.
Capillaries . . .	+ 15 to + 20 „ „
Small veins of arm . . .	+ 9 „ „
Portal vein	+ 10 „ „
Inferior vena cava . . .	+ 3 „ „
Large veins of neck	from 0 to − 8 „ „

(Starling.)

These pressures are, however, subject to considerable variations; the principal factors that cause variation are the following:—

Increase of *arterial* blood-pressure is produced by—

1. Increase in the rate and power of the heart-beat.
2. Increase in the contraction of the arterioles.
3. Increase in the total quantity of blood (plethora, after a meal, after transfusion).

Decrease in the *arterial* blood-pressure is produced by—

1. Decrease in the rate and force of the heart-beat.
2. Decrease in the contraction of the arterioles.
3. Decrease in the quantity of blood (*e.g.* after hæmorrhage).

The above is true for general arterial pressure; but if we are investigating local arterial pressure in any organ, the increase or decrease in the size of the arterioles of other areas may make its effect felt in the special area under investigation.

Venous pressure varies directly with the volume of the blood; in the arteries the effect of increase of fluid is slight and temporary, owing to the rapid adaptability of the peripheral resistance; the excess of fluid collects in and distends the easily dilatable venous reservoir. With regard to the first and second factors in the foregoing table, venous pressure varies in the opposite way to arterial pressure.

It is easy to understand how this is; when the *rate* of the heart increases, the total volume of blood discharged into the aorta per second is increased; similarly, an increase in the *force* of the beat also results in an increase in the cardiac output, and in both cases a more rapid and complete emptying of the auricle is produced. This is felt throughout the whole of the pulmonary circulation, and the accelerated flow therefore causes a fall in the venous pressure. If, however, the rise of pressure is due to a contraction of the arterioles, a stage may be reached in which the heart is no longer able to overcome the high pressure produced. It then fails to empty itself, and the blood is dammed up on the venous side, *i.e.* the venous pressure rises.

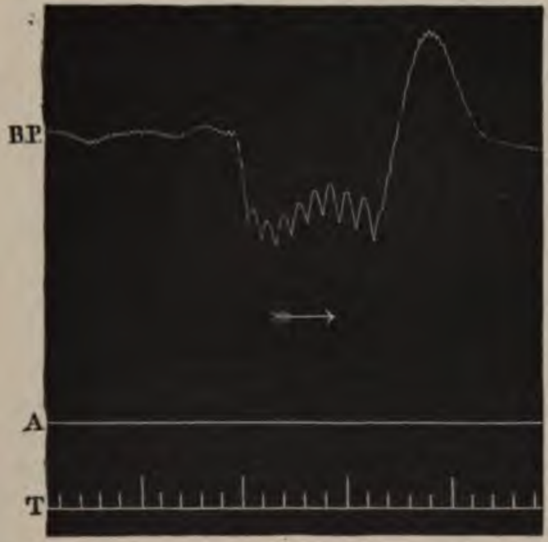

FIG. 277.—Effect of weak stimulation of the peripheral end of vagus on arterial blood-pressure (carotid of rabbit). BP, Blood-pressure; A, abscissa or base line; T, time in seconds. Note fall of blood-pressure and slow heart-beats.

With regard to the arterioles, contraction means a rise in arterial pressure, because while the amount sent into the arteries remains the same the outflow is cut down. More blood is therefore retained in them; they become more distended and the pressure rises. The first effect of this upon the venous pressure will be to diminish it, because if more blood is retained in the arteries there is less for the veins and capillaries. Also the rate of flow into the veins is at first decreased, and the venous pressure therefore falls. Moreover, the heart usually responds to a rise in pressure by increasing its force and rate, and consequently more blood is taken from the veins near actual experiment. They teach us that the highest pressure reached during systole may be twice or thrice the lowest attained during diastole.

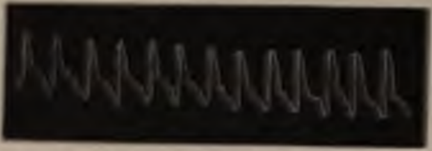

Fig. 216.—Normal arterial tracing obtained with Fick's Kymograph in the dog. (Burdon-Sanderson.)

The following table gives the probable average height of blood-pressure in various parts of the vascular system in man. They have been very largely inferred from experiments on animals:—

Large arteries (*e.g.* *carotid*) .	+ 140 mm. (about 6 inches) mercury.
Medium arteries (*e.g.* *radial*) .	+ 110 mm. mercury.
Capillaries . . .	+ 15 to + 20 " "
Small veins of arm . . .	+ 9 " "
Portal vein	+ 10 " "
Inferior vena cava . . .	+ 3 " "
Large veins of neck	from 0 to − 8 " "

(Starling.)

These pressures are, however, subject to considerable variations; the principal factors that cause variation are the following:—

Increase of *arterial* blood-pressure is produced by—

1. Increase in the rate and power of the heart-beat.
2. Increase in the contraction of the arterioles.
3. Increase in the total quantity of blood (plethora, after a meal, after transfusion).

Decrease in the *arterial* blood-pressure is produced by—

1. Decrease in the rate and force of the heart-beat.
2. Decrease in the contraction of the arterioles.
3. Decrease in the quantity of blood (*e.g.* after hæmorrhage).

The above is true for general arterial pressure; but if w investigating local arterial pressure in any organ, the in decrease in the size of the arterioles of other areas m effect felt in the special area under investigation.

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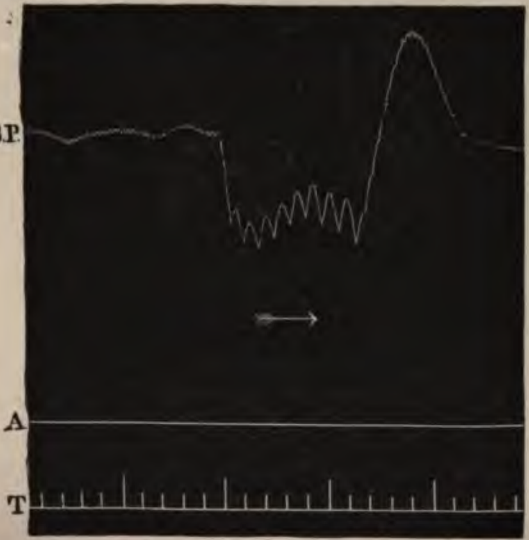

FIG. 277.—Effect of weak stimulation of the peripheral end of vagus on arterial blood-pressure (carotid of rabbit). BP, Blood-pressure; A, abscissa or base line; T, time in seconds. Note fall of blood-pressure and slow heart-beats.

Y[illegible] to the art[illegible] traction means a rise in arterial pr[illegible] while [illegible] ent into the arteries remains the [illegible] w is [illegible] blood is therefore retained in [illegible] pressure rises. The first [illegible] to diminish it, because [illegible] is less for the veins [illegible] the veins is at first [illegible] falls. Moreover, the [illegible] by increasing its force [illegible] from the veins [illegible] the heart. For both reasons, then, the venous pressure will fall, but that fall is limited, as pointed out above, to such an increase only as the heart is capable of overcoming successfully.

Capillary pressure is increased by—

1. Dilatation of the arterioles; the blood-pressure of the large arteries is then more readily propagated into them.

2. The size of the arterioles remaining the same, increase of arterial pressure from any other cause will produce a rise of capillary pressure.

3. By narrowing the veins leading from the capillary area; complete closure of the veins may quadruple the capillary pressure. This leads secondarily to an increased formation of lymph (dropsy); as when a tumour presses on the veins coming from the legs.

4. Any circumstance that leads to increased pressure in the veins will act similarly; this is illustrated by the effects produced by gravity on the circulation, as in alterations of posture.

Capillary pressure is decreased by the opposite conditions.

Capillary pressure is much more influenced by changes in the venous pressure, than by changes in the arterial pressure, since there is between the arteries and capillaries the variable and usually unknown peripheral resistance of the arterioles.

Effect of gravity on the circulation.—The main effect of gravity is that the veins are filled with blood in the part which is placed down. Thus, if an animal is placed suddenly with its legs hanging down, less blood will go to the heart, and the blood-pressure in the arteries will fall temporarily in consequence. This hydrostatic effect of gravity is soon overcome by an increased constriction of the vessels of the splanchnic area, when the vaso-motor mechanism is working normally. The efficient action of the "respiratory pump" is also of importance in counteracting gravity.

A very striking illustration of the effect of gravity on the circulation can be demonstrated on the eel. The animal is anæsthetised, and a small window is made in the body wall to expose the heart. If the animal is then suspended tail downwards, the beating heart is seen to be empty of blood; all the blood accumulates in the tail and lower part of the body; the animal has no "respiratory pump," such as a mammal possesses, to overcome the effects of gravity. If, however, the animal, still with its tail downwards, be suspended in a tall vessel of water, the pressure of the water outside its body enables it to overcome the hydrostatic effect of gravitation, and the heart-cavities once more fill with blood during every diastole. Another experiment originally performed by Salathe, can be demonstrated on a "hutch" rabbit. If the animal is held by the ears with its legs hanging down, it soon becomes unconscious, and if left in that position for about half an hour it will die. This is due to anæmia of the brain; the blood accumulates in the very pendulous abdomen which such domesticated animals acquire, and the vaso-motor mechanism of the splanchnic area is deficient in tone, and cannot be set into such vigorous action as is necessary to overcome the bad effects of gravity. Consciousness is, however, soon restored if the animal is placed in a horizontal position, or if while it is still hanging vertically the abdomen is squeezed or bandaged. A wild rabbit, on the other hand, suffers no inconvenience from a vertical position; it is a more healthy animal in every respect; its abdomen is not pendulous, and its vaso-motor power is intact. (Leonard Hill.)

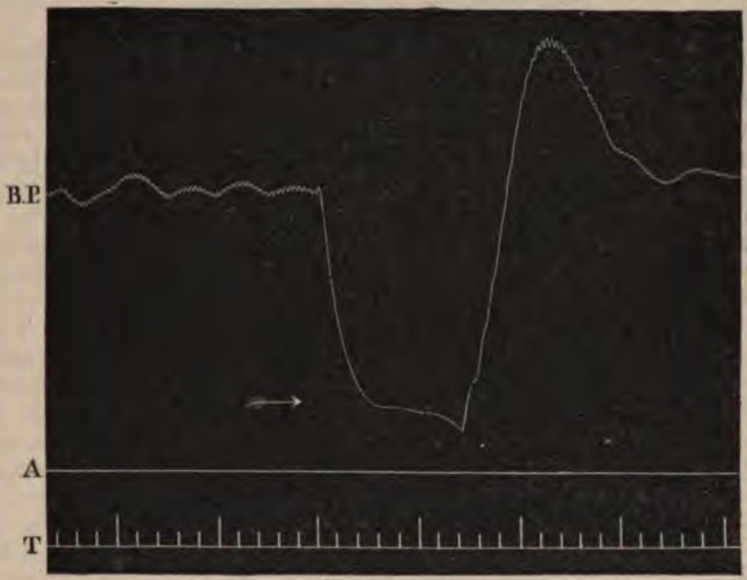

FIG. 278.—Effect of strong stimulation of the peripheral end of vagus on arterial blood-pressure (carotid of rabbit). Note stoppage of heart and fall of blood-pressure nearly to zero; after the recommencement of the heart, the blood-pressure rises, as in fig. 277, above the normal for a short time.

The pressure in the Pulmonary Circulation varies from $\frac{1}{3}$ to $\frac{1}{8}$ (mean $\frac{1}{6}$) of that in the systemic vessels.

The influence of the Cardiac Nerves on blood-pressure. The importance of the heart's action in the maintenance of blood-pressure is well shown by the effect that stimulation of the *vagus* nerve has on the blood-pressure curve. If the vagus of an animal is exposed and cut through, and the peripheral end stimulated, the result is that the heart is slowed or stopped; the arterial blood-pressure consequently falls; the fall is especially sudden and great if the heart is completely stopped. There is a rise in venous pressure. The effect on arterial pressure is shown in the two accompanying tracings; fig. 277 representing the effect of partial, and fig. 278 of complete stoppage of the heart; in both cases the animal used was a rabbit, and the artery the carotid.

On stimulating the cardiac *sympathetic* (accelerator and augmentor fibres) the increased action of the heart causes a rise of arterial pressure.

The effects of stimulating the central end of the vagus and other nerves cannot be understood until we have studied the vaso-motor nervous system.

The Velocity of the Blood-flow.

We have already seen that the velocity of the current of blood is inversely proportional to the sectional area of the bed through which it flows. The flow is, therefore, swiftest in the aorta and arteries, and slowest in the capillaries. In very round numbers, the rate is about a foot per second in the aorta, and about an inch per minute in the capillaries. The capacity of the veins is about twice or thrice that of the arteries; so the velocity in the veins is from a half to a third of that in the corresponding arteries. The rate in the veins increases as we approach the heart, as the total sectional area of the venous trunks becomes less and less.

The question of velocity is one of great importance, for it is on velocity that the actual amount of blood supplying the tissues mainly depends. In the capillaries the rate can be measured by direct microscopic investigation of the transparent portions of animals. E. H. Weber and Valentin were among the earliest to make these measurements in the frog, and the mean of their estimates gives the velocity as 25 mms. per minute in the systemic capillaries. In warm-blooded animals the velocity is somewhat greater; in the dog it is $\frac{1}{50}$ to $\frac{1}{100}$ inch (0·5 to 0·75 mm.) per second. It must be remembered that the total length of capillary vessels through which any given portion of blood has to pass probably does not exceed from $\frac{1}{50}$ to $\frac{1}{30}$ inch (0·5 mm.), and therefore the time required for each quantity of blood to traverse its own appointed portion of the general capillary system will scarcely amount to a second. It is during this time that the blood does its duties in reference to nutrition.

In the larger vessels direct observations of this kind are not possible, and it is necessary to have recourse to some instrumental method.

Volkmann was the first to make more or less accurate measurements by introducing a long U-shaped glass tube into the course of an artery. A diagram of this *hæmodromometer*, as it was termed, is shown in the accompanying diagram (fig. 279); this is filled with salt solution, and provided with a stop-cock *a*; this tap is so arranged that the blood can flow straight across from one section of the artery to the other; then at a given instant it is turned into the position shown in the diagram, and the blood has to traverse the long U-tube, and the time that it takes to traverse the tube, the length of which is known, is accurately observed. If the sectional area of the tube is the same as that of the artery, the velocity is obtained without further correction; but the difficulty of obtaining glass tubes with the exact calibre of every blood-vessel which one desires to experiment with led to the abandonment of this method, and Ludwig's *Stromuhr* (literally stream-clock) took its place. This consists of a U-shaped glass tube dilated at *a* and *a′*, the ends of which, *h* and *i*, are of known calibre. The bulbs can be filled by a common opening at *k*. The instrument is so contrived that at *b* and *b′*, the glass part is firmly fixed into metal cylinders, attached to a circular horizontal table *c c′*, capable of horizontal movement on a similar table *d d*, about the vertical axis marked in the figure by a dotted line. The openings in *c c′*, when the instrument is in position, as in fig. 280, corresponds exactly with those in *d d′*; but if *c c′* is turned at right angles to its present position, there is no communication between *h* and *a* and *i* and *a′*, but *h* communicates directly with *i*; and if turned through two right angles *c′* communicates with *d*, and *c* with *d′*, and there is no direct communication between *h* and *i*. The experiment is performed in the following way:—The artery to be investigated

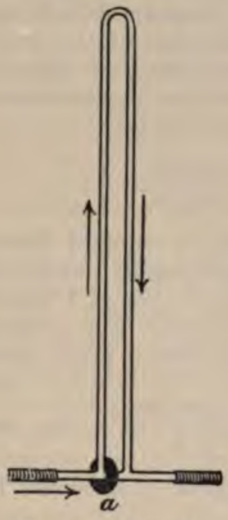

FIG. 279.—Volkmann's Hæmodromometer.

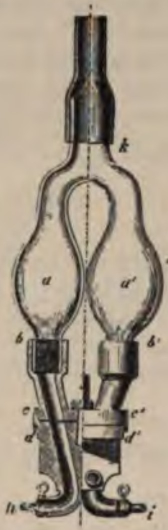

FIG. 280.—Ludwig's Stromuhr.

is divided and connected with two cannulæ and tubes which fit it accurately with *h* and *i*; *h* is the central end, and *i* the peripheral; the bulb *a* is filled with olive oil up to a point rather lower than *k*, and *a′* and the remainder of *a* is filled with defibrinated blood; the tube on *k* is then carefully clamped; the tubes *d* and *d′* are also filled with defibrinated blood. When everything is ready, the blood is allowed to flow into *a* through *h*, thus driving the oil over into *a′* and displacing the defibrinated blood through *i* into the peripheral end of the artery; *a′* is then full of oil; when the blood reaches the former level of the oil in *a*, the disc *c c′* is turned rapidly through two right angles, and the blood flowing through *d* into *a′* again displaces the oil, which is driven into *a*. This is repeated several times, and the duration of the experiment noted. The capacity of *a* and *a′* is known; the diameter of the artery is then measured, and as the number of times *a* has been filled in a given time is known, the velocity of the current can be calculated.

We may take an example to illustrate this:—

$$\text{Velocity} = \frac{\text{volume per second}}{\text{sectional area}} = \frac{\text{V}}{\text{S}}.$$

If the capacity of the bulb is 5 c.c., and it required 100 seconds to fill it 10 times, then the amount of blood passing through the instrument would be 50 c.c. in 100 seconds, or 0·5 c.c. in 1 second. Next, suppose the diameter of the artery is 4 mm. The sectional area is πr^2; r is the radius (2 mm.), and $\pi = 3{\cdot}1416$. From these data we get

$$\text{Velocity} = \frac{\text{V}}{\text{S}} = \frac{0{\cdot}5 \text{ c.c.}}{3{\cdot}1416 \times 2^2} = \frac{500 \text{ cubic millimetres}}{3{\cdot}1416 \times 4} = 39{\cdot}8 \text{ mm. per sec.}$$

Many modifications of Ludwig's original instrument have been devised. Fig. 281 shows Tigerstedt's.

The tubes A and B are placed in connection with the two ends of the cut artery as before; there is also a turn-table arrangement at F, by means of which the two upper tubes C and D may be connected as in the figure; or by twisting it through two right angles, D can be made to communicate with A, and C with B. In place of the two bulbs of Ludwig's instrument there is a glass cylinder H which contains a metal ball E. The whole instrument is washed out with oil to delay clotting, and filled with defibrinated blood. As soon as blood is allowed to flow from the artery, the ball E is driven over by the current till it reaches the other end of the cylinder; the instrument is then rapidly rotated through two right angles, and once more the ball is driven to the opposite end. This is repeated several times, and the number of revolutions during a given period is noted. The capacity of the cylinder *minus* that of the ball is ascertained, and the velocity is calculated by the same formula as that already given.

The Stromuhr has one advantage over the hæmodromometer, in that it enables one to note changes in *mean* velocity during the course of an experiment. The mean velocity varies very greatly even during a short experiment. Thus, in the carotid artery of a dog, the velocity of the stream varied from 350 to 730 mm. per second in the course of eighty seconds; in the same artery of the rabbit the variations were still more extensive (94 to 226 mm. per second—Dogiel).

Other instruments have been devised which give the variations in the velocity during the phases of the heart-beat; and some of these lend themselves to the graphic method, and give tracings of what is called the *velocity pulse*. Before we can understand these, it is necessary first to study the relationship of velocity to blood-pressure. Mere records of blood-pressure give us no indication of the velocity of the blood-stream; the latter depends, not on the absolute amount of pressure, but on the differences of pressure between successive points of the vascular system. When a fluid is in movement along a tube the forces maintaining the flow are two in number, the one *hydro-kinetic*, the other *hydro-static*. Thus, if we consider the flow from one point in the tube to another (say, for example, at 1 cm. distance), the force producing the flow are (1) the kinetic energy possessed by the blood when it enters the first spot (*i.e.* $\frac{mv^2}{2}$ dynes, or $\frac{mv^2}{2g}$ gramme-centimetres); and (2) the difference between the two lateral pressures at the two points in question. The important point to remember with respect to the part the pressure plays, is that the actual value of the lateral pressure does not matter, but that the resulting velocity, so far as pressure is concerned, depends only upon the fall of pressure between the two points. Therefore, the measurement to be determined is the rate of fall of pressure, or, as it is usually expressed, the *pressure gradient*. The steeper this gradient is, the more rapid is the flow. Thus, if an artery is suddenly cut across, the blood will spurt out at a far greater velocity than it possessed when flowing along the intact artery,

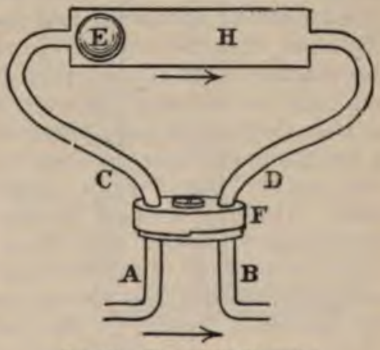

FIG. 281.—Tigerstedt's Stromuhr.

because the pressure gradient has been enormously increased in steepness. If, on the other hand, we suddenly cut across a vein along which the blood had been flowing at the same pace as in the intact artery first investigated, the flow will not be markedly accelerated, because the change in pressure gradient has not been increased to nearly so great an extent.

Again, the flow along a vein is just as rapid as along an artery of the same size, for although the actual pressure in the vein is much less, the pressure gradient is just as steep.

The influence of the kinetic factor is also of great importance in the consideration of the flow of blood along the arteries and veins. In the first place, it is obviously possible for the blood to flow from one point to another at a higher pressure if the kinetic energy at the first point is more than enough to compensate for the pressure increase. Under such circumstances the velocity at the second point must of course be less than that at the first. This implies, therefore, that the bed of the stream has widened, and under such circumstances the blood could actually flow *uphill*. In the case of the veins, as we have previously seen, the bed continuously narrows, so that this cannot take place; still it is possible to conceive such a condition to occur as that in which the blood from a well-filled vein empties into a more collapsed larger vein situated at a higher level. The one instance in which this effect is produced and is of great importance is in the filling of the auricles and ventricles. As these cavities fill, the blood comes to rest and so loses all kinetic energy; consequently the whole of the kinetic energy possessed by the blood flowing in the veins is converted into static energy, that is, into a pressure-head; in this way the cavities are distended to a much higher pressure than that in the great veins. The acute distension of the right auricle which follows any sudden failure of the right ventricle is brought about chiefly in this way.

It is usual to speak of the lateral pressure of the blood on the vessel wall as the *pressure-head*, and of the kinetic energy measured in terms of a pressure as the *velocity-head*. We could then say that the velocity between any two points is determined by the difference between the two pressure-heads *plus* the velocity-head at the first point. One method of recording the velocity-head is by the use of a tube (Pitot's tube) shaped as in the accompanying figure (fig. 282). The blood is made to enter at A, and leave through B; in the same straight line as A is a tube C, and a second tube D is placed at right angles to the tube B. If the tubes C and D are placed vertically and were sufficiently long, the blood would flow up C until it reached a height which would balance the pressure-head *plus* the velocity-head; in D it would only reach a height sufficient to balance the pressure-head; the difference in height between the two would therefore give the velocity-head. As the tubes would in this way be inconveniently long, it is better to use short tubes connected at the top by glass or rubber-tubing. The air contained will be compressed, and the two pressure-heads will balance one another, so that the difference in height will again represent the velocity-head; the velocity will be directly proportional to the square root of this velocity-head. This is the principle of one of the best instruments we possess for determining velocity, namely, Cybulski's photo-hæmatochometer. The meniscus of the fluid in each tube is photographed on a moving sensitive plate, and in this way a graphic record is obtained of the changes in velocity at times corresponding to different parts of the cardiac cycle. If one wishes to determine the velocity in absolute measures, the instrument must be previously calibrated by passing through it fluids flowing at known rates. It will be sufficient to give the results of one experiment; in the carotid artery during the ventricular systole the flow was at the rate of 238-248 mm. per second; during the diastole it sank to 127-156; in the femoral artery of the same animal, these numbers were 356 and 177 respectively.

To determine the pressure gradient in arteries, simultaneous measurements of the lateral pressures in two vessels at different distances from the heart must be recorded.

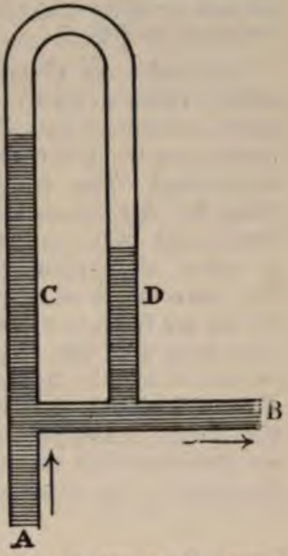

FIG. 282.—Diagram to illustrate the principle of Pitot's Tube and Cybulski's Photo-hæmatochometer.

It has been found that the diastolic pressures in the crural and carotid are practically identical, but that the maximum systolic pressure is actually higher in the crural than in the carotid; in the dog the difference may amount to as much as 60 mm. mercury. This difference is partly to be explained in that the carotid arises from the aorta at a right angle, and therefore gives the true pressure-head, while the crural, to a considerable extent, faces the stream, and therefore gives both pressure-head and velocity-head.

Unfortunately, at present no really satisfactory measurements are at hand from which the pressure gradient can be determined.

Cybulski's instrument is not the only one we possess for obtaining records of the velocity-pulse. Vierordt invented a hæmo-tachometer, employing the principle of the hydrometric pendulum; his instrument was improved by Chauveau. Chauveau's instrument is shown in fig. 283.

It consists of a thin brass tube, *a*, in one side of which is a small perforation closed by thin vulcanised indiarubber. Passing through the rubber is a fine lever, one end of which, slightly flattened, extends into the *lumen* of the tube, while the other moves over the face of a dial. The tube is inserted into the interior of an artery, and ligatures applied to fix it, so that the "*velocity pulse*," *i.e.*, the change of velocity with each heart-beat, may be indicated by the movement of the outer extremity of the lever on the face of the dial.

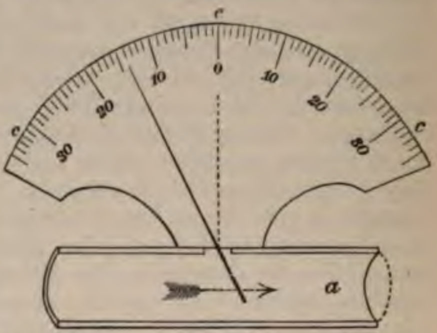

FIG. 283.—Diagram of Chauveau's Dromograph. *a*, Brass tube for introduction into the lumen of the artery, and containing an index needle, which passes through the elastic membrane in its side, and moves by the impulse of the blood current; *c*, graduated scale, for measuring the extent of the oscillations of the needle.

In order to obtain the actual value of these movements in terms of velocity, the instrument must be calibrated beforehand. The next diagram, fig. 284, shows how the instrument may be adapted to give a graphic record. The movements of the pendulum are brought to bear upon a tambour B, which communicates by a tube with the recording tambour C. If the mass of the pendulum is small, the accuracy of the instrument is considerable. Fig. 285 shows the tracing obtained from the carotid artery of the horse. The pressure curve is placed below it for purpose of comparison. The tracing shows the effects during the time corresponding to one cardiac cycle. On both curves the upstroke is the effect of the ventricular systole; this terminates at the apex of the first small curve (between the vertical lines 3 and 4) on the downstroke of the pressure curve, the rest of the downstroke until the commencement of the next systole (line 5) corresponds with the ventricular diastole. Beyond the line 4 is a larger secondary wave, which is known as the dicrotic wave; the smaller post-dicrotic waves

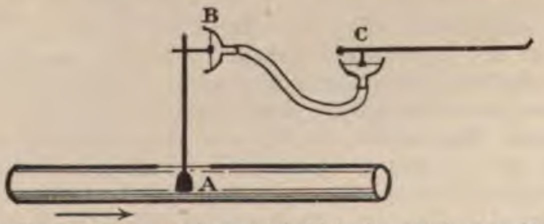

FIG. 284.—Chauveau's Dromograph connected with tambours to give a graphic record.

are due to elastic vibrations. We shall be studying all these points more in detail when we come to the pulse. When we compare the two curves together we note that the velocity curve reaches its maximum before the pressure curve; this is because, as the arteries become overfilled, the heart cannot maintain the initial velocity of output. The blood is thus forced along the arteries; then comes the diastole, and the recoil of the elastic arteries not only forces the blood onwards, but also produces a back-swing against the closed aortic valves; this produces the notch before the dicrotic wave; the blood is reflected from the aortic valves, once more producing a positive wave (the dicrotic wave). This affects both speed and pressure. It will be noticed that during the dicrotic notch the pressure falls comparatively little, but in the velocity curve the fall is considerable, and the curve sinks below the base line *oo*. This negative effect is naturally much more marked in the aorta and its first large branches than in situations further from the heart.

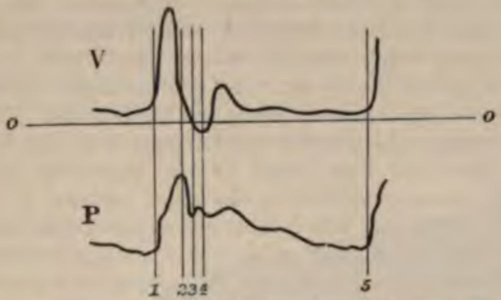

FIG. 285.—Velocity curve (V), and pressure curve (P) from the carotid artery of the horse; *oo*, abscissa of velocity curve; 1, 2, 3, 4 show simultaneous points on both curves. (Chauveau and Marey.)

In actual values Chauveau found that the velocity in the horse's carotid reached 520 mm. per second during systole; it sank to 220 at the time of the dicrotic wave, and to 150 during diastole.

The effect on the blood-flow of functional activity or vaso-motor changes has also been observed. Thus Lortet found that the carotid flow is five or six times greater when the horse is actively masticating than when it is at rest. After section of the cervical sympathetic, the lessening of the peripheral resistance raised the velocity from 540 to 750 mm. per second.

The Time of a Complete Circulation.

Among the earliest investigators of the question how long an entire circulation takes, was Hering. He injected a solution of potassium ferrocyanide into the central end of a divided jugular vein, and collected the blood either from the other end of the same vein, or from the corresponding vein of the other side. The substance injected is one that can be readily detected by a chemical test (the prussian blue reaction). Vierordt improved this method by collecting the blood as it flowed out, in a rotating disc divided into a number of compartments. The blood was tested in each compartment, and the ferrocyanide discovered in one which in the case of the horse received the blood about half a minute after the injection had been made. The experiment was performed in a large number of animals, and the following were a few of the results obtained:—

In the horse	31 seconds.
„ dog	16 „
„ cat	6·5 „
„ fowl	5 „

At first sight these numbers show no agreement, but in each case it was found that the time occupied was 27 heart-beats. The dog's heart, for instance, beats twice as fast as the horse's, and so the time of the entire circulation only occupies half as much time.

The question has recently been re-investigated by Stewart by improved methods, which have shown that the circulation time is considerably less than was found by the researches of Hering and Vierordt. The great objection to the older method is the fact that hæmorrhage is occurring throughout the experiment, and this would materially weaken the heart and slow down the circulation. Stewart has employed two methods. In the first, the carotid artery is exposed, and non-polarisable electrodes applied to it. These are placed in circuit with a cell, a galvanometer and one arm of a Wheatstone's bridge. After the resistances in the bridge have been balanced, and the galvanometer needle brought to rest, a small quantity of strong sodium chloride solution is injected into the opposite jugular vein. As soon as the salt reaches the carotid artery, the resistance of the blood is altered, the balance of the Wheatstone's bridge is upset, and the galvanometer needle moves. The period between the injection and the swing of the needle is accurately noted.

The second method used is even simpler, and gives practically the same results; a solution of methylene blue is injected into the jugular vein. The carotid artery on the opposite side is exposed, placed upon a sheet of white paper, and strongly illuminated. The time is noted between the injection and the moment when the blue colour is seen to appear in the artery. Stewart has applied these methods also for determining the time occupied by the passage of blood through various districts of the circulation; the longest circulation times were found in the kidney, the portal system, and the lower limbs. He calculates that the total circulation time in man is about 15 seconds.

None of these methods, however, give the true time of the entire circulation; they give merely the shortest possible time in which any particle of blood can travel through the shortest pathway. The blood that travels in the axial current, or which takes a broad pathway through wide capillaries, will arrive far more speedily at its destination than that which creeps through tortuous or constricted vessels. The direct observations of Tigerstedt on the output of the left ventricle show that the circulation time of the whole blood is at least five times as long as the period arrived at by the Hering method. It is therefore fallacious to use the circulation times arrived at by Hering's or Stewart's methods as a basis for calculating the total amount of the blood in the body.

The Pulse.

This is the most characteristic feature of the arterial flow. It is the response of the arterial wall to the changes in lateral pressure caused by each heart-beat.

A physician usually feels the pulse in the radial artery, since this is near the surface, and supported by bone. It is a most valuable indication of the condition of the patient's heart and vessels. It is necessary in feeling a pulse to note the following points:—

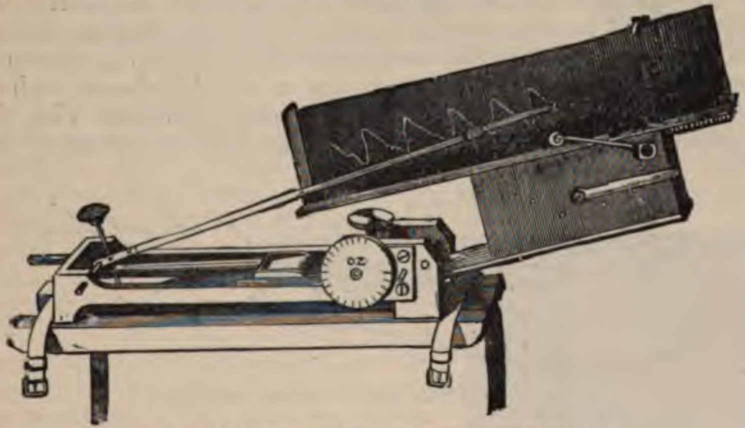

Fig. 286.—Marey's Sphygmograph, modified by Mahomed.

1. *Its frequency;* that is the number of pulse-beats per minute. This gives the rate of the heart-beats.
2. *Its strength;* whether it is a strong, bounding pulse, or a feeble beat; this indicates the force with which the heart is beating.

3. *Its regularity or irregularity;* irregularity may occur owing to irregular cardiac action either in force or in rhythm.
4. *Its tension;* that is the force necessary to obliterate it. This gives an indication of the state of the arterial walls and the peripheral resistance.

In disease there are certain variations in the pulse, of which we shall mention only two; namely, the *intermittent pulse,* due to the heart missing a beat every now and then; and the *water hammer* pulse, due either to aortic regurgitation or to a loss of elasticity of the arterial walls; either of these circumstances diminishes the onward flow of blood during the heart's diastole, and thus the suddenness of the impact of the blood on the arterial wall during systole is increased. When this condition is due to arterial disease, such as atheroma or calcification, this sudden pulse, combined with the decreased extensibility of the arteries, may lead to rupture of the walls, and this is especially serious if it occurs in the arteries of the brain (one cause of apoplexy).

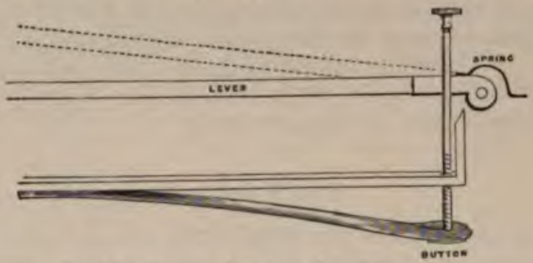

FIG. 287.—Diagram of the lever of the Sphygmograph.

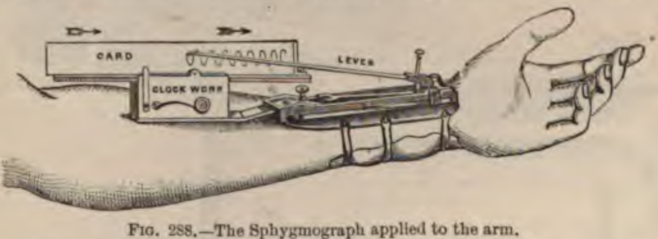

FIG. 288.—The Sphygmograph applied to the arm.

In order to study the pulse more fully, it is necessary to obtain a graphic record of the pulse-beat, and this is accomplished by the use of an instrument called the **sphygmograph**. This instrument consists of a series of levers, at one end of which is a button placed over the artery; the other end is provided with a writing-point to inscribe the magnified record of the arterial movement on a travelling surface.

The instruments most frequently used are those of Marey, one of the numerous modifications of which is represented in figures 286, 287, and 288, and of Dudgeon (fig. 289).

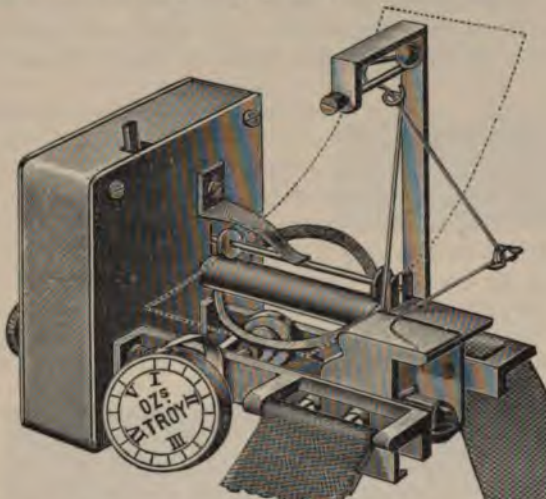

FIG. 289.—Dudgeon's Sphygmograph. The dotted outline represents the piece of blackened paper on which the sphygmogram is written.

Each instrument is provided with an arrangement by which the pressure can be adjusted so as to obtain the best record. The measurement of the pressure is, however, rough, and both instruments have the disadvantage of giving oscillations of their own to the sphygmogram; this is specially noticeable in Dudgeon's sphygmograph. But these defects may be overcome by the use of some form of sphygmometer. (See later, p. 292). It is also important to remember that the pad or button placed upon the artery rests partly on the venæ comites, so that not only arterial tension but any turgidity arising from venous congestion, will affect the height and form of the sphygmographic record.

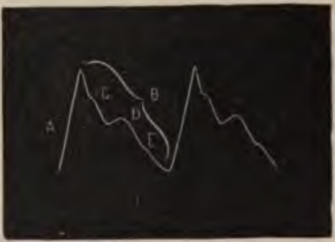

FIG. 290.—Diagram of pulse-tracing. A, upstroke; B, downstroke; C, pre-dicrotic wave; D, dicrotic; E, post-dicrotic wave.

Fig. 290 represents a typical sphygmographic tracing obtained from the radial artery. It consists of an upstroke due to the expansion of the artery, and a downstroke due to its retraction. The descent is more gradual than the upstroke, because the elastic recoil acts more constantly and steadily than the heart-beat. On the descent are several secondary (katacrotic) elevations.

A is the *primary*, or *percussion* wave; C is the *pre-dicrotic*, or *tidal* wave; D is the *dicrotic* wave, and E the *post-dicrotic* wave, and of these there may be several. In some rare cases there is a secondary wave on the upstroke, which is called an *anacrotic* wave (fig. 291).

These various secondary waves have received different interpretations, but the best way of explaining them is derived from information obtained by taking simultaneous tracings of the pulse, aortic pressure, apex beat, and intraventricular pressure, as in the researches of Hürthle. By this means it is found that the percussion and tidal waves occur during the systole of the heart, and the other waves during the diastole. The closure of the aortic valves occurs just before the dicrotic wave. The secondary waves on the downstroke other than the dicrotic are due to the elastic tension of the arteries, and are increased in number when the tension of the arteries is greatest. Some of the post-dicrotic waves are also doubtless instrumental in origin. The dicrotic wave has a different origin. It was at one time thought that this wave was due to a wave of pressure reflected from the periphery, but this view is at once excluded by the fact that wherever we take the pulse-tracing, whether from the aorta, carotid, radial, dorsalis pedis, or elsewhere, this secondary elevation always follows the percussion wave after the same interval, showing that it has its origin in the commencement of the arterial system. Moreover, a single pressure-wave reflected from the periphery would be impossible, as such a wave reflected from one part would be interfered with by those from other parts; moreover, a dicrotic elevation produced by a pressure-wave reflected from the periphery, would be increased by high peripheral resistance, and not diminished as is actually the case.

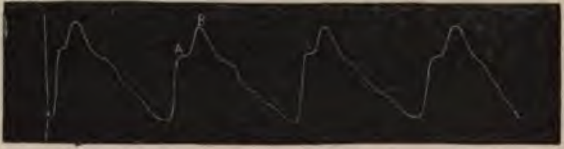

FIG. 291.—Anacrotic pulse.

The primary cause of the dicrotic wave is the closure of the semilunar valves; as already explained when we were considering the velocity pulse (p. 285), the inflow of blood into the aorta suddenly ceases, and the blood is driven back against the closed aortic doors by the elastic recoil of the aorta; the wave rebounds from these and is propagated through the arterial system as the dicrotic elevation. The production of the dicrotic wave is favoured by a low blood-pressure when the heart is beating forcibly, as in fever. Such a pulse is called a dicrotic pulse (fig. 292), and the second beat can be easily felt by the finger on the radial artery.

The percussion wave is produced by the ventricular systole expanding the artery. The sharp top at its summit is due to the sudden upward spring of the light lever of the sphygmograph. If it were possible to obtain a true record of what really occurs, we should doubtless have a tracing as shown by the continuous line in the accompanying figure (fig. 293). The apex of the tidal wave, B, marks the end of the ventricular systole.

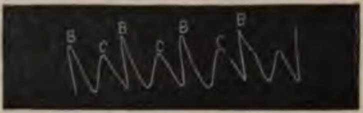

FIG. 292.—Dicrotic pulse.

In our study of intra-cardiac pressure, we saw that the systolic plateau sometimes has an ascending, sometimes a descending, slope (see p. 243); we now come to the explanation of this fact. If after the first sudden rise of pressure in the aorta the peripheral resistance is low, and the blood can be driven on from the aorta more rapidly than it is thrown in, the plateau will sink. If, on the other hand, the peripheral resistance is high, the aortic pressure will rise as long as the blood is flowing in, and we get an ascending systolic plateau and an anacrotic pulse. Thus an anacrotic pulse is seen in Bright's disease, where the peripheral resistance is very high.

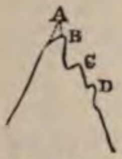

FIG. 293.—Diagram of pulse-tracing; A, percussion; B, tidal; C, dicrotic; and D, post-dicrotic waves.

If a long pulse-tracing is taken, the effect of the respiration can be seen causing an increase of pressure, and a slight acceleration of the heart's beats during inspiration.

The main waves of the pulse can be demonstrated without the use of any instrument at all by allowing the blood to spurt from a cut artery on to the surface of a large sheet of white paper travelling past it. We thus obtain what is very appropriately called a *hæmautograph* (fig. 294).

A distinction must be drawn between the pulse as felt at any one spot in the course of an artery, and the pulse-wave which is propagated throughout the arterial system. This wave of expansion travels along the arteries, and is started by the propulsion of the contents of the left ventricle into the already full arterial system. The more distant the artery from the heart, the longer the interval that elapses between the ventricular beat and the arrival of the pulse-wave. Thus it is felt in the carotid earlier than in the radial artery, and is still later in the dorsal artery of the foot. The difference of time is, however, very slight; it is only a minute fraction of a second; the wave travels at the rate of from 5 to 10 metres a second, that is twenty to thirty times the rate of the blood current.

The Rate of Propagation of the Pulse-Wave.—The method of ascertaining this may be illustrated by the use of a long elastic tube into which fluid is forced by the sudden stroke of a pump. If a series of levers are placed along the tube at measured distances those nearest the pump will rise first, those farthest from it last. If these are arranged to write on a revolving cylinder under one another, this will be shown graphically, and the time interval between their movements can be measured by a time tracing. The same principle is applied to the arteries of the body; a series of Marey's tambours are applied to the heart and to various arteries at known distances from the heart; their levers are arranged to write immediately under one another, as in fig. 248. The difference in time between the commencement of their upstrokes is measured by a time tracing in the usual way.

FIG. 294.—Hæmautograph, to be read from right to left.

The tracing taken with a sphygmograph is that of the pressure pulse; we may regard it as a blood-pressure tracing without a base line. The actual measurement of the blood-pressure in the human subject cannot obviously be effected by the apparatus employed on animals, and numerous instruments have been invented for the purpose which may be applied to the vessels without any dissection. One of the simplest of these *sphygmometers*, as they are termed, has been introduced by Hill and Barnard.

The instrument consists of a vertical glass tube about five inches in length, which expands above into a small bulb, and is closed at the top by a glass tap (see fig. 295). A small indiarubber bag is fixed to the tube below; this is surrounded by a metal cup, attached in such a way that only the base of the bag is exposed. The bag is filled with coloured fluid. On pressing the instrument down over the radial or other artery, the fluid rises in the tube and compresses the air in the bulb; the air acts as an elastic spring. The more one presses the more the fluid rises; at a certain height the meniscus of the fluid exhibits more pulsation than it does at any other height (*maximal pulsation*). The tube is empirically graduated in divisions that correspond to millimetres of mercury pressure. The point of maximal pulsation gives the arterial pressure. Before each observation the tap is opened, and by gentle pressure on the bag the fluid is set at the zero mark on the scale. Thus errors due to changes in barometric pressure or temperature are avoided.

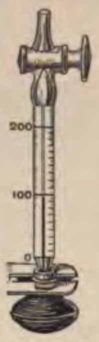

FIG. 295.—Hill and Barnard's Sphygmometer.

We now come to the explanation why the maximal pulsation gives us a reading of arterial pressure. If the mean pressure inside and outside an artery be made equal, then the wall of the vessel is able to vibrate at each pulse with the greatest freedom. The mean pressure is less than the systolic, but greater than the diastolic pressure; thus during the heart's systole the artery is opened out to its fullest extent, while during the heart's diastole its lumen is obliterated; hence the vessel wall swings with the greatest amplitude. If the pressure exerted by the sphygmometer is less than the mean arterial pressure, the artery will not be compressed to its utmost during diastole; if, on the other hand, the pressure exerted is greater than the mean, the artery will not fully expand during systole. In either case, the pulsation will not be so great as when the pressure exerted on the outside of the artery equals the mean pressure within.

By recording the arterial pressure in the dog with a mercury manometer and the sphygmometer simultaneously, the instrument has been found to give fairly accurate results (see note at end of this chapter, p. 313).

The normal pressure in the radial artery of healthy young adults is 110 to 120 mm. Hg. It appears to be as constant as the body temperature. In the recumbent posture the pressure is slightly lower than in the erect position. This relation is reversed in conditions of exhaustion. During muscular exertion the pressure is raised, while in the subsequent period of rest it is subnormal. Mental work raises the pressure; during rest and sleep it is lowered. The taking of food produces no noteworthy effect. In disease there are naturally variations in different directions, and the study of these has already yielded valuable results.

With this instrument the venous pressure can also be obtained in the manner suggested by Dr George Oliver. On the back of the hand or arm a vein is chosen free from anastomoses, and the sphygmometer is pressed upon the peripheral end of this. The vein is then emptied centrally—*i.e.*, towards the heart—by the pressure of the finger. Next the pressure in the sphygmometer is gradually relaxed, and the exact height noted at which the vein refills with blood.

Since the flow of blood through the capillaries is maintained by the difference in pressure between the artery and vein, we can, by obtaining readings both of the arterial and of the venous pressures, estimate the comparative efficiency of the capillary circulation in man under varying conditions.

The Capillary Flow.

When the capillary circulation is examined in any transparent part of a living animal by means of the microscope the blood is seen to flow with a constant equable motion; the red blood-corpuscles move along, mostly in single file, and bend in various ways to accommodate themselves to the tortuous course of the capillary, but instantly recover their normal outline on reaching a wider vessel.

At the circumference of the stream in the larger capillaries, and in the small arteries and veins, there is a layer of blood-plasma in contact with the walls of the vessel, and adhering to them, which moves more slowly than the blood in the centre. Anyone who has rowed on a river will know that the swiftest current is in the middle of the stream. The red corpuscles occupy the middle of the stream and move with comparative rapidity; the colourless corpuscles run much more slowly by the walls of the vessel; while next to the wall there is a transparent space in which the fluid is at comparative rest (the so-called "still layer"); if any of the corpuscles happen to be forced within it, they move more slowly than before, rolling lazily along the side of the vessel, and often adhering to its wall. Sometimes, when the motion of the blood is not strong, many of the white corpuscles collect in a capillary vessel, and for a time entirely prevent the passage of the red corpuscles.

When the peripheral resistance is greatly diminished by the dilatation of the small arteries, so much blood passes on from the arteries into the capillaries at each stroke of the heart, that there is not sufficient remaining in the arteries to distend them. Thus, the intermittent current of the ventricular systole is not converted into a continuous stream by the elasticity of the arteries before the capillaries are reached; and so intermittency of the flow occurs both in capillaries and veins, and a pulse is produced there. The same phenomenon may occur when the arteries become rigid from disease, and when the beat of the heart is so slow or so feeble that the blood at each cardiac systole has time to pass on to the capillaries before the next stroke occurs; the amount of blood sent out at each stroke is then insufficient to properly distend the elastic arteries.

It was formerly supposed that the occurrence of any transudation from the interior of the capillaries into the midst of the surrounding tissues was confined, in the absence of injury, strictly to the fluid part of the blood; in other words, that the corpuscles could not escape from the circulating stream, unless the wall of the containing blood-vessel was ruptured. Augustus Waller affirmed, in 1846, that he had seen blood-corpuscles, both red and white, pass bodily through the wall of the capillary vessel in which they were contained; and that, as no opening could be seen before their escape, so none could be observed afterwards—so rapidly was the part healed. But these observations did not attract much notice until the phenomenon was rediscovered by Cohnheim in 1867.

Cohnheim's experiment was performed in the following manner: A frog is curarised; and the abdomen having been opened, a portion of small intestine is drawn out, and its transparent mesentery spread out under a microscope. After a variable time, occupied by dilatation, following contraction of the minute vessels and accompanying quickening of the blood-stream, there ensues a retardation of the current, and blood-corpuscles begin to make their way through the capillaries and small vessels.

Diapedesis, or emigration of the white corpuscles, occurs to a small extent in health. But it is much increased in inflammation, and may go on so as to form a large collection of leucocytes (*i.e.* white corpuscles) outside the vessels.

The emigration of red corpuscles is only seen in inflammation, and is a passive process; it occurs when the holes made by the emigrating leucocytes do not close up immediately, and so the red corpuscles escape too.

The real meaning of the process of inflammation is a subject which is being much discussed now, but it may be interesting to state briefly the views of Metschnikoff, who has in recent years been a prominent investigator of the subject. Even if these views do not represent the whole truth, it can hardly be doubted that the phenomena described play a very important part in the process. Metschnikoff teaches that the vascular phenomena of inflammation have for their object an increase in the emigration of leucocytes, which have the power of devouring the irritant substance, and removing the tissues killed by the lesion. They are therefore called *phagocytes* (devouring or scavenging corpuscles). It may be that the microbic influence, or the influence of the chemical poisons they produce, is too powerful for the leucocytes; then they are destroyed, and the dead leucocytes become pus corpuscles; but if the leucocytes are successful in destroying the foreign body, micro-organisms, and disintegrated tissues, they disappear, wandering back to the blood-vessels, and the lost tissue is replaced by a regeneration of the surrounding tissues.*

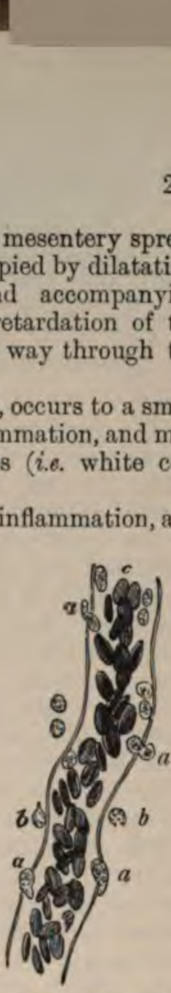

FIG. 296.—A large capillary from the frog's mesentery eight hours after irritation had been set up, showing emigration of leucocytes. *a*, Cells in the act of traversing the capillary wall; *b*, some already escaped. (Frey.)

The circulation through the capillaries must, of necessity, be largely influenced by that which occurs in the vessels on either side of them in the arteries or the veins; their intermediate position causes them to feel at once any alteration in the size, rate, or pressure of the arterial, and more especially of the venous blood-stream. The apparent contraction of the capillaries, on the application of certain irritating substances, and during fear, and their dilatation in blushing, may be referred primarily to the action of the small arteries.

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* This question is closely related to that of immunity, which is discussed in the chapter on the Blood (Chapter XXVI).

The Venous Flow.

The blood-current in the veins is maintained primarily by the *vis a tergo,* that is, the force behind, which is the blood-pressure transmitted from the heart and arteries; but very effectual assistance to the flow is afforded by the action of the muscles capable of pressing on the veins with valves, as well as by the suction action of the heart, and the aspiratory action of the thorax (*vis a fronte*).

The effect of muscular pressure upon the circulation may be thus explained. When pressure is applied to any part of a vein and the current of blood in it is obstructed, the portion behind the seat of pressure becomes swollen and distended as far back as the next pair of valves, which are in consequence closed (fig. 230, B, p. 220). Thus, whatever force is exercised by the pressure of the muscles on the veins, is distributed partly in pressing the blood onwards in the proper course of the circulation, and partly in pressing it backwards and closing the valves behind.

The circulation might lose as much as it gains by such an action, if it were not for the numerous communications which the veins make with one another; through these, the closing up of the venous channel by the backward pressure is prevented from being any serious hindrance to the circulation, since the blood, the onward course of which is arrested by the closed valves, can at once pass through some anastomosing channel, and proceed on its way by another vein. Thus, the effect of muscular pressure upon veins which have valves, is turned almost entirely to the advantage of the circulation.

In the web of the bat's wing, the veins are furnished with valves, and possess the remarkable property of *rhythmical contraction and dilatation,* whereby the current of blood within them is distinctly accelerated (Wharton Jones). The contraction occurs, on an average, about ten times in a minute; the existence of valves prevents regurgitation, so the entire effect of the contractions is auxiliary to the onward current of blood. Analogous phenomena have been observed in other animals.

A venous pulse is observed under the conditions previously described (p. 294), when the arterioles are dilated so that the arterial pulse passes through the capillaries to the veins.

A venous pulse is also seen in the superior and inferior vena cava near to their entrance into the heart; this corresponds to variations of the pressure in the right auricle. When the ventricle is contracting there is a slow rise due to the fact that the blood cannot get into the ventricle, and so distends the auricle; a second short, sharp elevation of pressure is produced by the auricular systole. Alterations of venous pressure are also produced in the great veins by the respiratory movements, the pressure sinking during inspiration, and rising during expiration.

The Vaso-Motor Nervous System.

The vaso-motor nervous system consists of the vaso-motor centre situated in the bulb, of certain subsidiary vaso-motor centres in the spinal cord, and of vaso-motor nerves, which are of two kinds—(*a*) those the stimulation of which causes constriction of the vessels; these are called *vaso-constrictor nerves;* (*b*) those the stimulation of which causes dilatation of the vessels; these are called *vaso-dilator nerves.*

The following names are associated with the history of the subject. The muscular structure of arteries was first described by Henle in 1841; in 1852 Brown Séquard made a study of the vaso-constrictor, or, as he termed them, tonic nerves. The vaso-motor centre was discovered by Schiff (1855), and more accurately localised by Ludwig (1871). The dilator nerves were also discovered by Schiff; at first they were termed paretic nerves. Other names which must be mentioned in connection with the subject are those of Claude Bernard, Heidenhain, and, in more recent years, Gaskell, Langley, and Ramon y Cajal.

The nerves supply the muscular tissue in the walls of the blood-vessels and regulate their calibre, but exert their most important action in the vessels which contain relatively the greatest amount of muscular tissue, namely, the small arteries or arterioles.

Under ordinary circumstances, the arterioles are maintained in a state of moderate or tonic contraction, and this constitutes the peripheral resistance, the use of which is to keep up the arterial pressure, which must be high enough to force the blood through the capillaries and veins in a continuous stream back to the heart.

Another function which is served by this muscular tissue is to regulate the amount of blood which flows through the capillaries of any organ in proportion to its needs. During digestion, for instance, it is necessary that the digestive organs should be supplied with a large quantity of blood: for this purpose the arterioles of the splanchnic area are relaxed, and there is a vast amount of blood in this area, and therefore a correspondingly small amount in other areas, such as the skin; this accounts for the sensation of chilliness experienced after a full meal. The skin vessels form another good example; one of the most important uses of the skin is to get rid of the heat of the body in such a way that the body temperature shall remain constant; when excess of heat is produced there is also an increase in the loss of heat; the skin vessels are then dilated, and so more blood is exposed on the surface, and thus an increase in the radiation of heat from the surface is brought about. On the other hand, when it is necessary that the heat produced should be kept in the body, the loss of heat is diminished by a constriction of the skin vessels, as in cold weather. The alteration of the calibre of the vessels is brought about by the action of the vaso-motor nervous system on the muscular tissue of the arterioles.

There are certain organs of the body in which the necessity for alterations in their blood-supply does not exist. Such organs are the lungs and the brain. It is in the vessels of these organs that the influence of vaso-motor nerves is at a minimum. The pulmonary vessels are stated by Bradford and Dean to be supplied by nerves which leave the cord in the upper thoracic region; but on stimulating these the rise of pressure produced is extremely small; it is very doubtful if the fibres in question are really vaso-constrictors; the small rise observed may be partly or even wholly due to the acceleration of the heart, which is another result of stimulating these nerve-roots.

The *vaso-motor centre* lies in the grey matter of the floor of the fourth ventricle; it is a few millimetres in length, reaching from the upper part of the floor to within about 4 mm. of the calamus scriptorius. The position of this centre has been discovered by the following means: when it is destroyed the tone of the small vessels is no longer kept up, and in consequence there is a great and universal fall in arterial blood-pressure; when it is stimulated there is an increase in the constriction of the arterioles all over the body, and therefore a rise of arterial blood-pressure. Its upper and lower limits have been accurately determined in the following way: a series of animals is taken, and the central nervous system divided in a different place in each; the cerebrum and cerebellum may be cut off without affecting blood-pressure, the vaso-motor centre must therefore be below these; if the section is made just above the medulla, the blood-pressure still remains high, and it is not till the upper limit of the centre is passed that the blood-pressure falls. Similarly, in another series of animals, if the cervical cord is cut through, and the animal kept alive by artificial respiration, there is an enormous fall of pressure due to the influence of the centre being removed from the vessels; in other experiments the section is made higher and higher, and the same result noted, until at last the lower limit of the centre is passed, and the fall of pressure is less and less marked the higher one goes there, until in the animal in which the section is made at the upper boundary of the centre the blood-pressure is not affected at all, and the centre can be influenced reflexly by the stimulation of afferent nerves, the pressor and depressor nerves, which we shall be considering immediately.

After the destruction of the vaso-motor centre in the bulb, there is a fall of pressure. If the animal is kept alive, the vessels after a time recover their tone, and the arterial pressure rises; it rises still more on stimulating the central end of a sensory nerve; this is due to the existence of subsidiary vaso-motor centres in the spinal cord; for on the subsequent destruction of the spinal cord the vessels again lose their tone and the blood-pressure sinks.

The vaso-motor path is down the lateral column of the spinal cord, and the fibres terminate by arborising around the cells in the grey matter of the subsidiary vaso-motor centres, the anatomical position of which is uncertain, though it is probably in the cells of the intermedio-lateral tract. From these cells fresh axis-cylinder processes originate, which pass out as the small medullated nerve-fibres in the anterior roots of the spinal nerves.

The *vaso-constrictor* nerves for the whole body leave the spinal cord by the anterior roots of the spinal nerves from the second thoracic to the second lumbar, both inclusive. They leave the roots by the white rami communicantes, and pass into the ganglia of the sympathetic chain, which lies on each side along the front of the vertebral column. The ganglia on this chain (the lateral ganglia of Gaskell) may also be called the chain of vaso-motor ganglia, because here are situated cell stations on the course of the vaso-constrictor nerves for the head, trunk and limbs. That is to say, the small medullated nerve-fibres terminate by arborising around the cells of these ganglia, and a fresh relay of axis-cylinder processes from these cells carry on the impulses.

The next figure (fig. 297) represents diagrammatically how this occurs. The sheaths of the fibres are not represented.

The cell station of any particular fibre is not necessarily situated in the first ganglion to which it passes; the fibres of the white ramus communicans of the second thoracic do not, for instance, all have their cell stations in the corresponding thoracic ganglion, but may pass upwards or downwards in the chain to a more or less distant ganglion before they terminate by arborising around a cell or cells.

The vaso-constrictor nerves, however, have all cell stations somewhere in the sympathetic system, and the new axis-cylinders that arise from the cells of the ganglia differ from those which terminate there in the circumstance that they do not possess a medullary sheath, but they are pale, grey, or non-medullated fibres. Those which are destined for the supply of the vessels of the head and neck pass into the ganglion stellatum or first thoracic ganglion, thence through the annulus of Vieussens to the inferior cervical ganglion, and thence along the sympathetic trunk to their destination. Their cell station is in the superior cervical ganglion.

Those for the body wall and limbs pass back from the sympathetic ganglia to the spinal nerves by the grey rami communicantes, and are distributed with the other spinal nerve-fibres. The cell stations for the upper limb fibres are in the ganglion stellatum, and for the lower limb fibres in the lower lumbar and upper sacral ganglia.

Those for the interior of the body pass into the various plexuses of sympathetic nerves in the thorax and abdomen, and are distributed to the vessels of the thoracic and abdominal viscera. This set includes the most important vaso-motor nerves of the body, the splanchnics. Their cell stations are situated in the various ganglia of the abdominal plexuses.

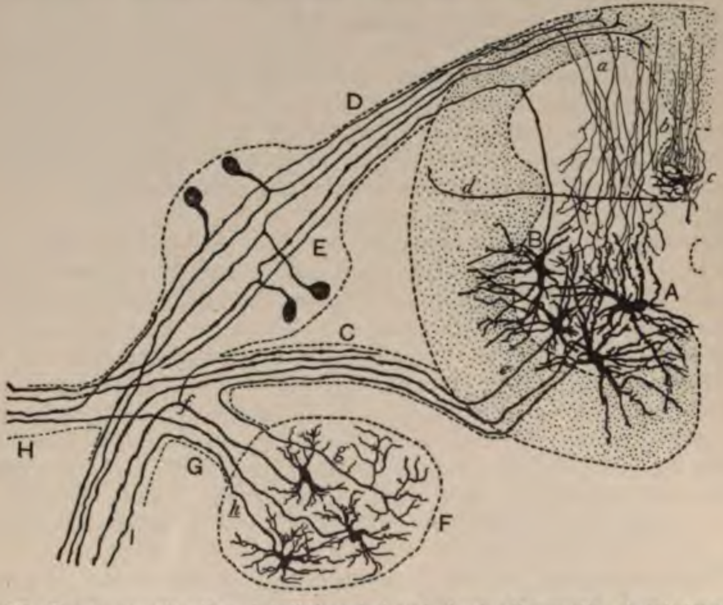

FIG. 297.—Transverse section through half the spinal cord, showing the ganglia. A, anterior cornual cells; B, axis-cylinder process of one of these going to posterior root; C, anterior (motor) root; D, posterior (sensory) root; E, spinal ganglion on posterior root; F, sympathetic ganglion; G, ramus communicans; H, posterior branch of spinal nerve; I, anterior branch of spinal nerve; *a*, long collaterals from posterior root fibres reaching to anterior horn; *b*, short collaterals passing to Clarke's column; *c*, cell in Clark's column sending an axis-cylinder (*d*) process to the direct cerebellar tract; *e*, fibre of the anterior root; *f*, axis-cylinder from sympathetic ganglion cell, dividing into two branches, one to the periphery, the other towards the cord; *g*, fibre of the anterior root terminating by an arborisation in the sympathetic ganglion; *h*, sympathetic fibre passing to periphery. (Ramon y Cajal.)

The *vaso-dilator* nerves in part accompany those just described, but they are not limited to the outflow from the second thoracic to the second lumbar. Thus, the nervi erigentes originate as white rami communicantes from the second and third sacral nerves, and the chorda tympani, another good example of a vaso-dilator nerve, is a branch of the seventh cranial nerve. Bayliss has also shown that the posterior root fibres may act as vaso-dilators (see p. 303).

All vaso-motor nerves, whether they are constrictor or dilator, differ very markedly from the spinal nerve-fibres which are distributed to voluntary muscles in being ganglionated; that is, in having cell stations or positions of relay on their course from the central nervous system to the muscular fibres they supply.

The existence of cell stations between the central nervous system and the muscular fibres is not confined to the nerves of blood-vessels, but is found also in the nerves which supply the heart and other viscera.

Moreover, the nerves which supply the voluntary muscles are motor in function; inhibitory fibres to the voluntary muscles of vertebrates do not exist. But in the case of the involuntary muscles there are usually the two sets of nerve-fibres with opposite functions.

In the case of the heart, we have an accelerator set which course through the sympathetic, and an inhibitory set which course through the vagus.

In the case of the vessels, we have an accelerator set, which we have hitherto called vaso-constrictors, and an inhibitory set we have been calling vaso-dilators.

In the case of the other contractile viscera, we have also viscero-accelerator and viscero-inhibitory, which respectively hasten and lessen their peristaltic movements.

Adopting Gaskell's nomenclature, we may further term the accelerator groups of nerves *katabolic*, as they increase the activity of the muscles they supply, bringing about an increase of wear and tear, and an increase in the discharge of waste material. The inhibitory nerves, on the other hand, are *anabolic*, as they produce a condition of rest in the tissues they supply, and so give an opportunity for repair or constructive metabolism.

The distribution of the vaso-motor nerves and the viscero-motor nerves has been within recent years very thoroughly worked out by Langley. The nerves of the various viscera we shall take with the individual organs. In all these cases, there is a cell station somewhere in the sympathetic system, and only one for each nerve-fibre. The *preganglionic fibres* (*i.e.*, the fibres from the spinal cord to the sympathetic cell station) are usually medullated; the *postganglionic fibres* (*i.e.*, those that leave the ganglion) are usually non-medullated. But this histological distinction, so much emphasised by Gaskell, is not without exceptions, and the localisation of cell stations is made with far greater certainty by Langley's nicotine method. Nicotine in small doses paralyses nerve-cells,[*] but not nerve-fibres; if the drug is injected into an animal, stimulation of the anterior nerve-roots produces no movements of the involuntary muscles, because the paralysed cell stations on the course of the nerve-fibres act as blocks to the propagation of the impulses. If the nicotine is applied locally by painting it over one or more ganglia, there will be a block in those fibres only which have their cell stations in those particular ganglia. Thus, in the lateral chain of ganglia we find the cells on the course of the pilo-motor nerves (*i.e.*, to the muscles of the hairs), of the vaso-constrictors of the head, limbs, and body walls, and possibly of the splenic nerves. In the collateral ganglia (*i.e.*, cœliac, mesenteric, etc.) are found, amongst others, the cells on the course of the splanchnic nerves, of the nerves to sweat glands, of the cardiac accelerators, and of the inhibitory fibres of the alimentary canal; while in the terminal ganglia are placed, among others, the cells on the course of the cardiac inhibitory nerves, of the motor fibres to the lower part of the intestine and bladder, and of the inhibitory fibres to the external genital organs.

We may now ask what is the object that is served by the existence of ganglia on the course of these nerves. It appears to be a means of distributing nerve-fibres to a vast area of muscular tissue by means of a comparatively small number of nerve-fibres that leave the central nervous system; for each fibre that leaves the central nervous system arborises around a number of cells, and thus the impulse it carries is transferred to a large number of new axis-cylinder processes.

In some cases, it is true, a single nerve-fibre will divide into multitudinous branches to accomplish the same object (as in the supply of the electric organ of Malapterurus, the fibres to the millions of its subdivisions all originating from a single axis-cylinder), but the usual way appears to be a combination of this method with that of subsidiary cell-stations.

At one time a ganglion was supposed to be the normal centre for reflex action. The submaxillary ganglion was the battle-field in which this question was fought out in Claud Bernard's time. In the later researches of Langley and Anderson, the only instances where such a thing seemed possible were the following:—When all the nervous connections of the inferior mesenteric ganglion are divided except the hypogastric nerves, stimulation of the central end of one hypogastric causes contraction of the bladder, the efferent path to which is the other hypogastric nerve. In addition, they observed an apparent reflex excitation of the nerve supplying the erector muscles of the hairs (pilo-motor nerves) through other sympathetic ganglia. In neither case is the action truly reflex, but is caused by the stimulation of the central ends of motor-fibres which issue from the spinal cord, and which after passing through the ganglion send branches down each hypogastric nerve. The experiment is in fact similar to Kühne's gracilis experiment (p. 173).

It certainly is the case that under normal circumstances, the centres for reflex action are in the central nervous system. But there do appear to be some conditions in which it is possible for ganglia to assume this function. The recovery of vaso-motor tone, and of tone in certain viscera after destruction of extensive tracts of the spinal cord, or the persistence of peristaltic action in the intestine after cutting through all its nerves, are cases in point. (See further, under Intestinal Movements, and Spinal Visceral Reflexes).

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[*] It is still a matter of uncertainty whether this drug acts upon the nerve-cells themselves, or the terminal arborisations (synapses) of the nerve-fibres that surround them. Before the paralytic effect of nicotine comes on, it excites the nerve-cells, and thus in the case of the blood-vessels causes a general constriction of the arterioles and a rise of arterial pressure.

The observations of W. M. Bayliss on the vaso-dilator nerves of dogs are of considerable interest. He could find no vaso-dilator fibres to the hind limb in the abdominal sympathetic chain; but the only fibres excitation of which produced vascular dilatation there, are contained in the posterior roots. He also found fibres in the posterior roots of the 12th and 13th thoracic nerves, which act as vaso-dilators of the small intestine. Not only is vaso-dilatation the result of mechanical, electrical, or thermal stimulation of these roots, but experiments are adduced which show that in normal reflexes, such as occur when the depressor nerve is stimulated, the dilator impulses travel by the same route. This raises the question whether the posterior roots contain true efferent fibres. The facts of degeneration show that they do not. Bayliss is therefore driven to the conclusion that the same nerve terminations in the periphery serve both to take up sensory impressions, and to convey inhibitory impulses to the muscular structures in which they end. In other words, we have here another example which may be added to those previously mentioned (p. 173), that nerve-fibres may convey impulses in both directions. The term *antidromic* is used by Bayliss to express the fact that impulses may travel in the reverse direction to that in which they usually pass.

The Vaso-motor centre can be excited directly, as by induction currents; the result is an increase of arterial blood-pressure owing to an increase of the contraction of the peripheral arterioles.

It can also be excited by the action of *poisons* in the blood which circulates through it; thus, strophanthus or digitalis causes a marked rise of general arterial pressure due to the constriction of the peripheral vessels brought about by impulses from the centre.

It is also excited by venous blood, as in *asphyxia;* the rise of blood-pressure which occurs during the first part of asphyxia is due to constriction of peripheral vessels; the fall during the last stage of asphyxia is largely due to heart failure. We shall study asphyxia more at length in connection with respiration. During the period of decreased pressure, waves are often observed on the blood-pressure curve which arise from a slow rhythmic action of the vaso-motor centre. The centre alternately sends out stronger and weaker constrictor impulses. They are known as the *Traube-Hering* waves, and are much slower in their rhythm than the waves on the tracing which are due to respiration. They are not peculiar to asphyxia, but are frequently seen in tracings from normal animals. Fig. 298 represents tracings obtained from a dog under the influence of morphine and curare. The upper curve, taken while artificial respiration was being carried on, shows the three sets of waves, first the oscillations due to the heart-beats, next in size those due to the respiratory movements, which in their turn are superposed on the prolonged Traube-Hering waves. The lower tracing was taken immediately after the cessation of the artificial respiration, and shows only the heart-beats and the Traube-Hering waves.

The Vaso-motor centre may be excited reflexly.—The afferent

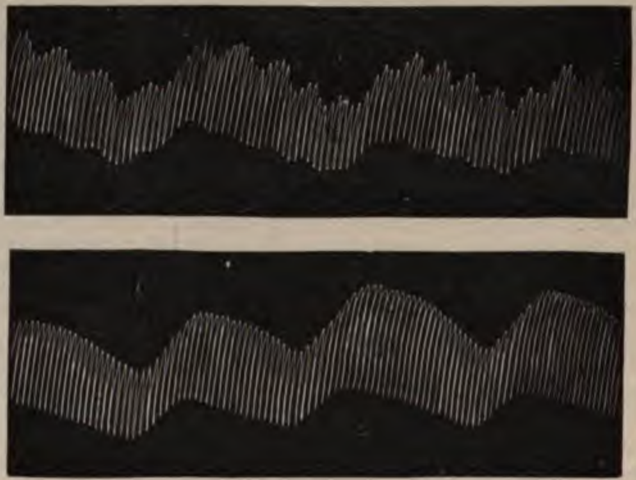

FIG. 298.—Arterial blood-pressure tracings showing Traube-Hering waves. (Starling.)

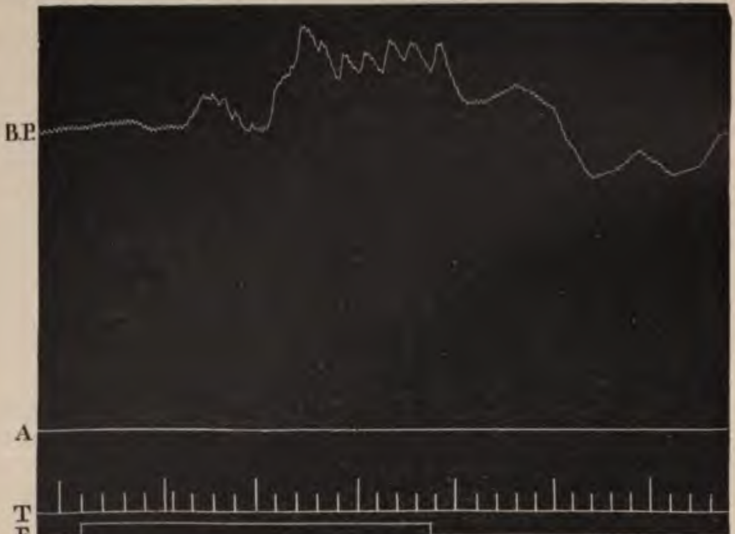

FIG. 299.—Result on arterial blood-pressure curve of stimulating the central end of cut sciatic nerve in rabbit. BP, blood-pressure; A, abscissa or base line; T, time in seconds; E, signal of period of excitation of the nerve.

impulses to the vaso-motor centre may be divided into **pressor** and **depressor**.

Most sensory nerves are *pressor* nerves. The sciatic or the vagus nerves may be taken as instances; when they are divided and their central ends stimulated, the result is a rise of blood-pressure due to the stimulation of the vaso-motor centre, and a consequent constriction of the arterioles all over the body, but especially in the splanchnic area. Fig. 299 shows the result of such an experiment. It is necessary in performing such an experiment to administer curare as well as an anæsthetic to the animal, in order to obviate reflex muscular struggles, which would themselves produce a rise in arterial pressure.

Many sensory nerves also contain *depressor* fibres which produce the opposite effect. The most marked bundle of these is known as *the depressor nerve.* In most animals this is bound up in the trunk of the vagus; but in some, like the rabbit, cat, and horse, the nerve runs up as a separate branch from the heart (or, according to some recent observations, from the commencement of the aorta), and joins the vagus or its superior laryngeal branch, and ultimately reaches the vaso-motor centre. When this nerve is stimulated (the vagi having been previously divided to prevent reflex inhibition of the heart), a marked fall of arterial blood-pressure is produced (see fig. 300). Stimulation of this nerve affects the vaso-motor centre in such a way that the normal constrictor impulses that pass down the vaso-constrictor nerves are inhibited. The fall of pressure is very slight after section of the splanchnic nerves, showing that the splanchnic area is the part of the body most affected. The normal function of this nerve is to adapt the peripheral resistance to the heart's action: if the constriction of the arterioles is too high for the heart to overcome, an impulse by this nerve to the vaso-motor centre produces reflexly a lessening of the peripheral resistance.

N.B.—The term depressor should be carefully distinguished from inhibitory; stimulation of the peripheral end of the vagus produces a fall of blood-pressure due to inhibition (slowing or stoppage) of the heart (see figs. 277 and 278); stimulation of the central end of the depressor nerve produces a lowering of blood-pressure for a different reason, namely, a reflex relaxation of the splanchnic arterioles.

Experiments on Vaso-motor nerves.—The experiments on the vaso-motor nerves are similar to those performed on other nerves when one wishes to ascertain their functions. They consist of section and excitation.

Section of a vaso-constrictor nerve, such as the splanchnic, causes a loss of normal arterial tone, and consequently the part supplied by the nerve becomes flushed with blood. Stimulation of the peripheral end causes the vessels to contract and the part to become comparatively pale and bloodless. This can be very readily demonstrated on the ear of the rabbit. This is a classical experiment associated with the name of Claude Bernard. Division of the cervical sympathetic produces an increased redness of the side of the head, and looking at the ear, the transparency of which enables one to follow the phenomena easily, the central artery with its branches is seen to become larger, and many small branches not previously visible come into view. The ear feels hotter, though this effect soon passes off as the exposure of a large quantity of blood to the air causes a rapid loss of heat. On stimulating the peripheral end of the cut nerve, the ear resumes its normal condition, and then becomes paler than usual owing to excessive constriction of the vessels.

The first part of the experiment, the dilatation following section, can be demonstrated in a very simple way, by pressing the thumb-nail forcibly on the nerve where it lies by the side of the central artery of the ear.

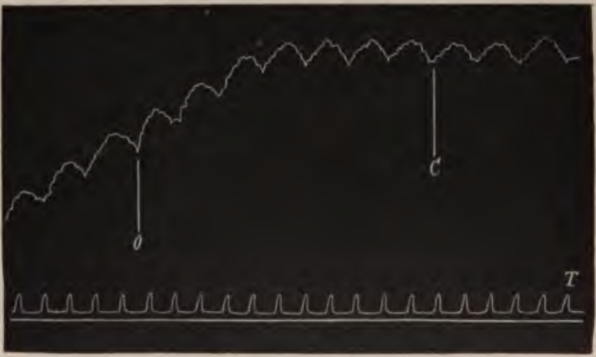

FIG. 300.—Tracing showing the effect on blood-pressure of stimulating the central end of the Depressor nerve in the rabbit. To be read from right to left. T, indicates the rate at which the recording-surface was travelling, the intervals correspond to seconds; C, the commencement of faradisation of the nerve; O, moment at which excitation was discontinued. The effect is some time in developing, and lasts after the current has been taken off. The larger undulations are the respiratory curves; the pulse oscillations are very small. (Foster.)

Section of a vaso-dilator nerve, such as the chorda tympani, produces no effect on the vessels, but stimulation of its peripheral end causes great enlargement of all the arterioles, so that the submaxillary gland and the neighbouring parts supplied by the nerve become red and gorged with blood, and the pulse is propagated through to the veins; the circulation through the capillaries is so rapid that the blood loses very little of its oxygen, and is therefore arterial in colour in the veins. Another effect, free secretion of saliva, we shall study in connection with that subject.

Other examples of vaso-dilator nerves are the nervi erigentes to the erectile tissue of the penis, etc., and of the lingual nerve to the vessels of the tongue.

It is, however, probable that all the vessels of the body receive both constrictor and dilator nerves. But the presence of the latter is difficult to determine unless they are present in excess; if they are not, stimulation affects the constrictors most. The effect of section is also inconclusive; for if a mixed nerve is cut, the only effect observed is a dilatation due to removal of the tonic constrictor influence.

To solve this difficult problem, three methods are in use:—

1. *The method of degeneration.*—If the sciatic nerve is cut, the vessels of the limb dilate. This passes off in a day or two. If the peripheral end of the nerve is then stimulated, the vessels are dilated, as the constrictor fibres degenerate earliest, and so one gets a result due to the stimulation of the still intact dilator fibres.

2. *The method of slowly interrupted shocks.*—If a mixed nerve is stimulated with the usual rapidly interrupted faradic current, the effect is constriction; but if the induction shocks are sent in at long intervals (*e.g.*, at intervals of a second), vaso-dilator effects are obtained. This can be readily demonstrated on the kidney vessels by stimulation of the anterior root of the eleventh thoracic nerve in the two ways just indicated.

By studying the rate of flow of the blood through the submaxillary gland, in which the vaso-constrictor and dilator fibres run separate courses, it has been shown that if both sets of fibres are simultaneously excited, constriction is produced during the stimulation, while marked dilatation follows after the stimulation has ceased. Excitation of the constrictors alone is not followed by dilatation. These results explain the mode of action of slowly interrupted shocks, for with each there will only be a very slight constriction, while the dilator effects which run a much slower course will be summed up to produce a marked effect.

3. *The influence of temperature.*—Exposure to a low temperature depresses the constrictors more than the dilators. If the leg is placed in ice-cold water, stimulation of the sciatic, even if it has only been recently divided, produces a flushing of the skin with blood.

Plethysmography.

The action of vaso-motor nerves can be studied in another way than by the use of various forms of manometer, which is the only method we have considered so far. The second method, which is often used together with the manometer, consists in the use of an instrument which records variations in the volume of any limb, or organ of an animal. Such an instrument is called a **plethysmograph.** One of these instruments applied to the human arm is shown in the accompanying figure (fig. 301).

Every time the arm expands with every heart's systole, a little of the fluid in the plethysmograph is expelled and raises the lever. Variations in volume due to respiration are also seen in the tracing. An air plethysmograph connected to a sensitive recorder gives equally good results.

The same instrument in a modified form applied to such organs as the spleen and kidney is generally called an **oncometer**, and the recording part of the apparatus, the **oncograph.** These instruments we owe to Roy, and the next two figures represent respectively sections of the kidney oncometer and oncograph.

An oncometer consists of a metal capsule, of shape suitable to enclose the organ: its two halves are jointed together, and fit accurately except at one opening which is left for the vessels of the organ. A delicate membrane is attached to the rim of each half, the space between which and the metal is filled with warm oil. The tube from the oncometer is connected to the oil-containing cavity of the oncograph by a tube also containing oil. An increase in the volume of the organ squeezes the oil out of the oncometer into the oncograph, and so produces a rise of the oncograph piston and lever; a contraction of the organ produces a fall of the lever.

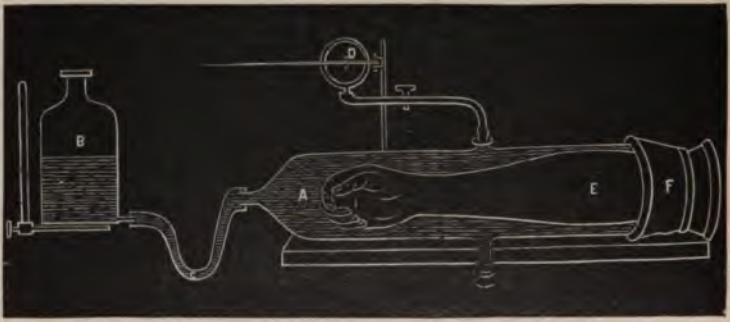

FIG. 301.—Plethysmograph. By means of this apparatus, the alteration in volume of the arm, E, which is enclosed in a glass tube, A, filled with fluid, the opening through which it passes being firmly closed by a thick gutta-percha band, F, is communicated to the lever, D, and registered by a recording apparatus. The fluid in A communicates with that in B, the upper limit of which is above that in A. The chief alterations in volume are due to alteration in the blood contained in the arm. When the volume is increased, fluid passes out of the glass cylinder, and the lever, D, also is raised, and when a decrease takes place the fluid returns again from B to A. It will therefore be evident that the apparatus is capable of recording alterations of the volume of blood in the arm.

Very good results are obtained by using saline solution instead of oil; and Schafer has shown in connection with the spleen that a spleen box of simple shape covered with a glass plate, made air-tight with vaseline, and communicating by a tube with a Marey's tambour, gives a far more delicate record of the splenic alterations of volume than the oil oncometer.

If now we are investigating the action of the anterior root of eleventh thoracic nerve on the vessels of the kidney, a tracing is taken simultaneously of the arterial blood-pressure in the carotid, and of

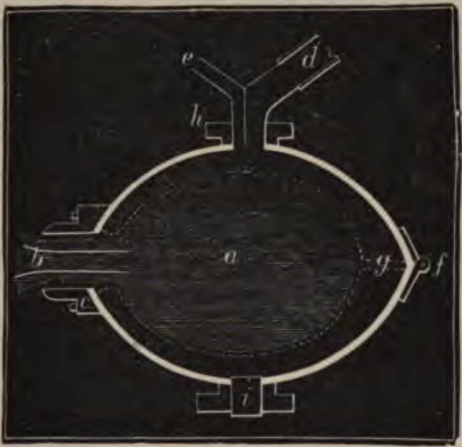

FIG. 302.—Diagram of Roy's Oncometer. *a*, represents the kidney enclosed in a metal box, which opens by hinge *f*; *b*, the renal vessels and duct. Surrounding the kidney are two chambers formed by membranes, the edges of which are firmly fixed by being clamped between the outside metal capsule, and one (not represented in the figure) inside, the two being firmly screwed together by screws at *h*, and below. The membranous chamber below is filled with a varying amount of warm oil, according to the size of the kidney experimented with, through the opening, then closed with the plug *i*. After the kidney has been enclosed in the capsule, the membranous chamber above is filled with warm oil through the tube *e*, which is then closed by a tap (not represented in the diagram); the tube *d* communicates with a recording apparatus, and any alteration in the volume of the kidney is communicated by the oil in the tube to the chamber *d* of the Oncograph, fig. 303.

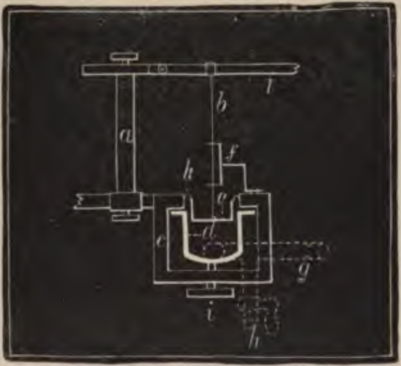

FIG. 303.—Roy's Oncograph, or apparatus for recording alterations in the volume of the kidney, etc., as shown by the oncometer—*a*, upright, supporting recording lever *l*, which is raised or lowered by needle *b*, which works through *f*, and which is attached to the piston *e*, working in the chamber *d*, with which the tube from the oncometer communicates. The oil is prevented from being squeezed out as the piston descends by a membrane, which is clamped between the ring-shaped surfaces of cylinder by the screw *i* working upwards; the tube *h* is for filling the instrument.

the volume of the kidney by the oncometer. On stimulating the nerve rapidly, there is a slight rise of arterial pressure, but a large fall of the oncograph lever, showing that the kidney has diminished in volume. It is evident that there must be an active contraction of the arterioles of the kidney, causing it to diminish in size, for the blood-pressure tracing (which is taken as a control to be sure the changes are not otherwise produced) shows that there is no failure of the heart's activity to account for it.

We shall return to the subject of the oncometer in connection with the spleen and the kidney. We may, however, say in passing what a very important experimental method plethysmography is becoming. Since the introduction of air oncometers, the method is remarkably easy to apply, and it is now part of the routine practice of physiologists, when they are investigating the action of a drug, or of a nerve, on any organ, to record its volume changes by the plethysmographic method. Thus, the salivary glands, lobes of the liver or lung, the limbs, the kidney, spleen, a coil of intestine, etc., can all be easily enclosed in an appropriately shaped gutta-percha box, covered with a glass plate made air-tight with vaseline. There are always two openings to such a box, one to allow the vessels and nerves to enter (leakage of air around these is prevented by packing with cotton-wool soaked in vaseline); the other opening is filled up with a piece of glass tubing which is connected by an indiarubber tube to the recording apparatus. The most delicate of the volume recorders is the bellows-recorder of Brodie (see p. 152) and the piston recorder of Hürthle; a Marey's tambour is not so sensitive, and, moreover, it is a recorder of pressure rather than of volume only.

Of all the oncometers, I am inclined to believe that the intestinal oncometer is the most instructive, because the coil of intestine under observation gives a truer record of what is occurring in that important area called the splanchnic area, than any other abdominal organ.

Pathological Conditions.

The vaso-motor nervous system is influenced to some extent by conditions of the cerebrum, some emotions, such as fear, causing pallor (vaso-constriction), and others causing blushing (vaso-dilatation).

It is almost impossible to over-estimate the importance of the study of vaso-motor phenomena, as a means of explaining certain pathological conditions; our knowledge of the processes concerned in *inflammation* is a case in point.

Disorders of the vessels due to vaso-motor disturbances are generally called *angio-neuroses.* Of these we may mention the following:—

Tache cérébrale is due to abnormal sensitiveness of the vascular nerves; drawing the finger-nail across the skin causes an immediate *wheal*, or at least a red mark that lasts a considerable time. At one time this was considered characteristic of affections of the cerebral meninges like tubercular meningitis, and was consequently called the "meningeal streak." It, however, occurs in a variety of pathological conditions of the nervous system, both cerebral and spinal.

In certain conditions which lead to *angina pectoris* the pain in the heart is in part due to its being unable to overcome an immense peripheral resistance, and the condition is relieved by the administration of drugs like amyl-nitrite or nitro-glycerin, which relax the vessels and cause universal blushing.

Raynaud's disease is one in which there is a localised constriction of the vessels which is so effectual as to entirely cut off the blood supply to the capillary areas beyond, and if this lasts any considerable time may lead to gangrene of the parts in question.

Local Peculiarities of the Circulation.

The most remarkable peculiarities attending the circulation of blood through different organs are observed in the cases of the *brain*, *erectile organs*, *lungs*, *liver*, *spleen*, and *kidneys*.

In the Brain.—The brain must always be supplied with blood, for otherwise immediate loss of consciousness would follow. Hence, to render accidental obliteration almost impossible, four large arteries are supplied to the brain, and these anastomose together in the circle of Willis. The two vertebral arteries are, moreover, protected in bony canals. Two of the brain arteries can be tied in monkeys, and three or even all four in dogs, without the production of serious symptoms. In the last case enough blood reaches the brain by branches from the superior intercostal arteries to the anterior spinal artery. The sudden obliteration of one carotid artery in man may in some cases produce epileptiform spasms; the sudden occlusion of both occasions loss of consciousness. Uniformity of supply is further ensured by the arrangement of the vessels in the pia mater, in which, previous to their distribution to the substance of the brain, the large arteries break up and divide into innumerable minute branches ending in capillaries, which, after frequent communication with one another, enter the brain and carry into nearly every part of it uniform and equable streams of blood. The arteries are enveloped in a special lymphatic sheath. The arrangement of the veins within the cranium is also peculiar. The large venous trunks or sinuses are formed so as to be scarcely capable of change of size; and composed, as they are, of the tough tissue of the dura mater, and, in some instances, bounded on one side by the bony cranium, they are not compressible by any force which the fulness of the arteries might exercise through the substance of the brain; nor do they admit of distension when the flow of venous blood from the brain is obstructed. No valves are placed between the vertebral veins and the vena cava; the vertebral veins anastomose with the cerebral sinuses. Hence on squeezing the thorax and abdomen, venous blood can be pressed from those parts out of any opening made into the longitudinal sinus. Expiration acts in the same way; it raises the cerebral venous pressure; if the skull wall is defective the brain expands owing to the distension of its capillaries during the expiratory act. The exposed brain also expands with each systole of the heart. Owing to the fact that the brain lies enclosed in the cranium, the arterial pulse is transmitted through the brain substance to the cerebral veins, and so the blood issues from these in pulses.

Since the brain is enclosed in the rigid cranium the volume of blood in the cerebral vessels cannot alter unless the volume of the other cranial contents alters in the opposite sense.

These conditions of the brain and skull led Monro and Kellie many years ago to advance the opinion that the quantity of blood in the brain must be the same at all times. This doctrine has been frequently disputed, and many have advanced the theory that increase or diminution of the blood is accompanied with simultaneous diminution or increase of the cerebro-spinal fluid, so that the contents of the cranium are kept uniform in volume. But the recent work of Leonard Hill has shown that the Monro-Kellie doctrine is in the main true. Histological evidence has recently been obtained of the existence of nerve plexuses round the pial arteries. The arteries are muscular, and the nerves therefore are most probably vaso-motor in function. Experimental evidence so far, however, has not established that the action of these nerves is a marked one*; the cerebral circulation passively follows the slightest changes in aortic and, more especially, vena cava pressure, and no active vaso-motor change has been conclusively proved. The velocity of blood-flow through the brain is thus influenced markedly by the condition of the vessels of the splanchnic area. If the tone of the skeletal muscles and that of the vessels be suddenly inhibited by fear, or temporarily destroyed by shock the blood will drop owing to its weight into the dilated and supported vessels in the most dependent parts of the body. The flow of blood through the brain will, under these conditions, cease, that is to say, so long as the body is in the erect posture. Thus, to restore a fainting person the head must be lowered between the knees. Muscular exercise, by returning blood to the heart from the veins of the lower parts of the body, conduces to the maintenance of an efficient cerebral circulation.

It is not the volume of the blood but the velocity of flow which is altered in the brain by changes in the general circulation. The brain with its circulating blood almost entirely fills the cranial cavity in the living animal; that is, there is no more cerebro-spinal fluid there than is sufficient to moisten the membranes. Cerebro-spinal fluid escapes into the veins at any pressure above the cerebral venous pressure; the tension of this fluid and the pressure in the veins are therefore always the same. The fluid probably transudes from the vascular fringes of the choroid plexuses in the ventricles of the brain, and is absorbed by the pial veins. There is not enough of this absorbable fluid present to allow of more than a slight increase of the volume of blood in the brain. If the aortic pressure rises and the vena cava pressure remains constant the conditions in the brain are as follows:—

More blood in the arteries, less in the veins, increased velocity of flow.

While if the aortic pressure remains constant and the vena cava pressure rises, the conditions are:—

Less blood in the arteries, more in the veins, diminished velocity of flow.

The brain presses against the cranial wall with a pressure equal to that in the cerebral capillaries. A foreign body introduced within the cranium, such as a blood-clot or depressed bone, produces local anæmia of the brain, by occupying the room of the blood. So soon as the capillaries are thus obliterated the pressure is raised to arterial pressure. This local increase of cerebral tension cannot be transmitted by the cerebro-spinal fluid, because this fluid can never be retained in the meningeal spaces at a tension higher than that of the cerebral veins, but is immediately re-absorbed. The anatomical arrangements of the tentorium cerebelli and the falciform ligaments are such as to largely prevent the transmission through the brain-substance of a local increase of pressure. There is complete pressure discontinuity between the cranial and vertebral cavities. The serious results that follow cerebral compression are primarily due to obliteration of the blood-vessels, and consequent anæmia of the brain. A very small foreign body will, if situated in the region of the bulb, produce the gravest symptoms. For the centres which control the vascular and respiratory systems are rendered anæmic thereby. The cerebral hemispheres may, on the other hand, be compressed to a large extent without causing a fatal result. The major symptoms of compression arise as soon as any local increase of pressure is transmitted to the bulb and causes anæmia there.

In Erectile Structures.—The instances of greatest variation in the quantity of blood contained, at different times, in the same organs, are found in certain structures which, under ordinary circumstances, are soft and flaccid, but, at certain times, receive an unusually large quantity of blood, become distended and swollen by it, and pass into the state which has been termed *erection*. Such structures are the *corpora cavernosa* and *corpus spongiosum* of the penis in the male, and the *clitoris* in the female; and, to a less degree, the *nipple* of the mammary gland in both sexes. The corpus cavernosum penis, which is the best example of an erectile structure, has an external fibrous membrane or sheath; and from the inner surface of the latter are prolonged numerous fine lamellæ which divide its cavity into small compartments. Within these is situated the plexus of veins upon which the peculiar erectile property of the organ mainly depends. It consists of short veins which very closely interlace and anastomose with each other in all directions, and admit of great variations of size, collapsing in the passive state of the organ, but capable of an amount of dilatation which exceeds beyond comparison that of the arteries and veins which convey the blood to and from them. The strong fibrous tissue lying in the intervals of the venous plexuses, and the external fibrous membrane or sheath with which it is connected, limit the distension of the vessels, and during the state of erection, give to the penis its condition of tension and firmness. The same general condition of vessels exists in the corpus spongiosum urethræ, but around the urethra the fibrous tissue is much weaker than around the body of the penis, and around the glans there is none. The venous blood is returned from the plexuses by comparatively small veins. For all these veins one condition is the same; namely, that they are liable to the pressure of muscles when they leave the penis. The muscles chiefly concerned in this action are the erector penis and accelerator urinæ. Erection results from the distension of the venous plexuses with blood. The principal exciting cause in the erection of the penis is nervous irritation, originating in the part itself, and derived reflexly from the brain and spinal cord. The nervous influence is communicated to the penis by the pudic nerves, which ramify in its vascular tissue; and after their division the penis is no longer capable of erection.

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* The only experimental evidence yet adduced as to the functional activity of these nerves is contained in the work of Ferrier and Brodie. They perfused defibrinated blood through a recently excised brain, and found that the addition of adrenalin to the blood always produced constriction of the vessels and a lessened blood flow.

Erection is not complete, nor maintained for any time except when, together with the influx of blood, the muscles mentioned contract, and by compressing the veins, stop the efflux of blood, or prevent it from being as great as the influx.

The circulation in the Lungs, Liver, Spleen and Kidneys will be described in our study of those organs.

Sphygmometers.

The disadvantage which the Hill-Barnard sphygmometer (p. 292) possesses, is that in order to press it upon the radial artery, the base of the elastic bag no longer possesses its usual curvature, and thus some of the pressure recorded is employed in an attempt to reduce the deformation of the shape of the bag: the pressure recorded is thus too high. A better instrument is the modification of the Riva Rocci apparatus devised by C. J. Martin. It consists of an elastic bag about three inches wide, which is wrapped around the arm, covered with a sheet of lead and firmly strapped on. Air is forced into the bag by a tube leading from a simple pump; this tube is also connected by a side branch to a mercury manometer. As one continues to pump and distend the bag, the pressure on the arm is increased until a point is reached when the pulse at the wrist is no longer felt. The pressure necessary to do this is equal to the systolic pressure, and is simultaneously registered by the manometer.

CHAPTER XXII

LYMPH AND LYMPHATIC GLANDS

As the blood circulates through the capillary blood-vessels, some of its liquid constituents exude through the thin walls of these vessels, carrying nutriment to the tissue elements. This exudation is called *lymph;* it receives from the tissues the products of their activity, and is collected by the lymph channels, which converge to the thoracic duct—the main lymphatic vessel—and thus the lymph once more re-enters the blood-stream near to the entrance of the large systemic veins into the right auricle.

Lymph is a fluid, which comes into much more intimate relationship with metabolic processes in the tissues than the blood; in fact, there is only one situation—the spleen—where the blood comes into actual contact with the elements—that is, cells, fibres, etc.—of a tissue.

Composition of Lymph.

Lymph is alkaline; its specific gravity is about 1015, and after it leaves the vessels it clots, forming a colourless coagulum of fibrin. It is like blood-plasma in composition, only diluted so far as its proteid constituents are concerned. This is due to the fact that proteids do not pass readily through membranes. The proteids present are called *fibrinogen, serum globulin,* and *serum albumin;* these we shall study with the blood-plasma. The salts are similar to those of blood-plasma, and are present in the same proportions. The waste products, like carbonic acid and urea, are more abundant in lymph than in blood. The total amount of solids dissolved in lymph is about 6 per cent., more than half of which is proteid in nature.

When examined with the microscope the transparent lymph is found to contain colourless corpuscles, which are called *lymphocytes;* these are cells with large nuclei and comparatively little protoplasm. They pass with the lymph into the blood, where they undergo growth, and are called *leucocytes.*

All the lymphatics pass at some point of their course through lymphatic glands, which are the factories of these corpuscles. Lymphocytes also pass into the lymph stream wherever lymphoid tissue is found, as in the tonsils, thymus, Malpighian bodies of the spleen, Peyer's patches, and the solitary glands of the intestine. The lymph that leaves these tissues is richer in lymph-cells than that which enters them.

When lymph is collected from the thoracic duct after a meal containing fat, it is found to be milky. This is due to the presence in the lymph of minutely subdivided fat particles absorbed from the interior of the alimentary canal. The lymph is then called *chyle.* The fat particles constitute what used to be called the *molecular basis* of chyle. If the abdomen is opened during the process of fat absorption, the lymphatics are seen as white lines, due to their containing this milky fluid. They are consequently called *lacteals.*

The structure and arrangement of the lymphatic vessels are given in Chapter XVIII., and we have now to study the structure of

The Lymphatic Glands.

Lymphatic glands are round or oval bodies varying in size from a hemp-seed to a bean, interposed in the course of the lymphatic vessels, and through which the lymph passes in its course to be discharged into the blood-vessels. They are found in great numbers in the mesentery, and along the great vessels of the abdomen, thorax, and neck; in the axilla and groin; a few in the popliteal space, but not further down the leg, and in the arm as far as the elbow.

A lymphatic gland is covered externally by a capsule of connective-tissue, generally containing some unstriped muscle. At the inner side of the gland, which is somewhat concave (*hilus*), (fig. 304), the capsule sends inwards processes called *trabeculæ* in which the blood-vessels are contained, and these join with other processes prolonged from the inner surface of the part of the capsule covering the convex or outer part of the gland; they have a structure similar to that of the capsule, and entering the gland from all sides, and freely communicating, form a fibrous scaffolding. The interior of the gland is seen on section, even when examined with the naked eye, to be made up of two parts, an outer or *cortical*, which is light coloured,

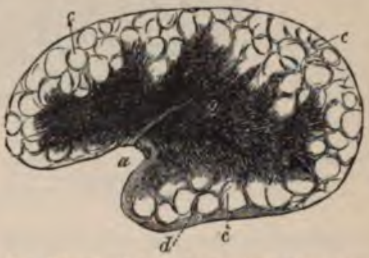


FIG. 304.—Section of a mesenteric gland from the ox, slightly magnified. *a*, Hilus; *b* (in the central part of the figure), medullary substance; *c*, cortical substance with indistinct alveoli; *d*, capsule. (Kölliker.)

and an inner or *medullary* portion of redder appearance (figs. 304, 305). In the outer part, or cortex, of the gland (fig. 305), the intervals between the trabeculæ are large and regular; they are termed *alveoli;* whilst in the more central or medullary part is a finer meshwork formed by an irregular anastomosis of the trabecular processes. Within the alveoli of the cortex and in the meshwork formed by the trabeculæ in the medulla, is contained lymphoid tissue; this occupies the central part of each alveolus; but at the periphery, surrounding the central portion and immediately next the capsule and trabeculæ, is a more open meshwork of retiform tissue constituting the *lymph-path,* and containing but few lymph-corpuscles. At the inner part of the alveolus, the central mass divides into two or more smaller rounded or cord-like masses which, joining with those from the other alveoli, form a much closer arrangement than in the cortex; spaces (fig. 306, *b*) are left within those anastomosing cords, in which are found portions of the trabecular meshwork and the continuation of the lymph-path.

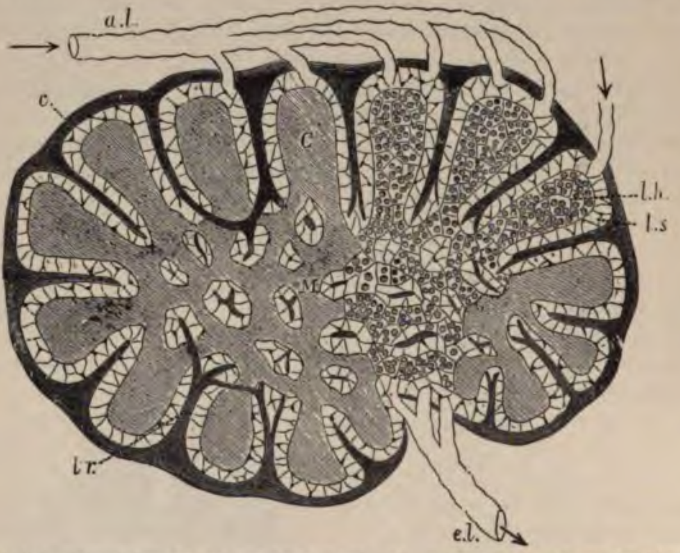


FIG. 305.—Diagrammatic section of lymphatic gland. *a.l.*, afferent; *e.l.*, efferent lymphatics; *C*, cortical substance; *l.h.*, lymphoid tissue; *l.s.*, lymph-path; c., fibrous capsule sending in trabeculæ *tr.* into the substance of the gland. (Sharpey.)

The lymph enters the gland by several afferent vessels, which pierce the capsule and open into the lymph-path; at the same time they lay aside all their coats except the endothelial lining, which is continuous with the lining of the lymph-path. The *efferent* vessels begin in the medullary part of the gland, and are continuous with the lymph-path here as the afferent vessels are with the cortical portion.

The efferent vessels leave the gland at the *hilus*, and either at once, or very soon after, join together to form a single vessel.

Blood-vessels which enter and leave the gland at the hilus are freely distributed to the trabecular and lymphoid tissues.

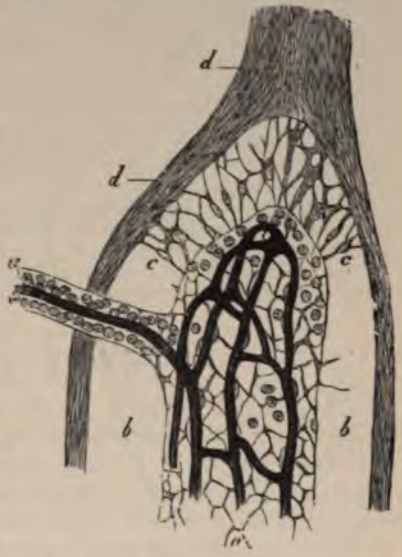


FIG. 306.—A small portion of medullary substance from a mesenteric gland of the ox. *d*, *d*, trabeculæ; *a*, part of a cord of lymphoid tissue from which all but a few of the lymph-corpuscles have been washed out to show its supporting meshwork of retiform tissue and its capillary blood-vessels (which have been injected, and are dark in the figure); *b*, *b*, lymph-path, of which the retiform tissue is represented only at *c*, *c*, × 300. (Kölliker.)

The Lymph Flow.

The flow of the lymph towards the point of its discharge into the veins is brought about by several agencies. With the help of the valvular mechanism all occasional pressure on the exterior of the lymphatic and lacteal vessels propels the lymph onward; thus muscular and other external pressure accelerates the flow of the lymph as it does that of the blood in the veins. The action of the muscular fibres of the small intestine, and the layer of unstriped muscle present in each intestinal villus, assist in propelling the chyle; in the small intestine of a mouse, the chyle has been seen moving with intermittent propulsions that correspond with the peristaltic movements of the intestine. But, for the general propulsion of the lymph and chyle, it is probable that, together with the *vis a tergo* resulting from external pressure, some of the force is derived from the contractility of the vessel's own walls. The respiratory movements, also, favour the current of lymph through the thoracic duct as they do the current of blood in the thoracic veins.

Lymph-Hearts.—In amphibia, reptiles and some birds, an important auxiliary to the movement of the lymph and chyle is supplied in certain muscular sacs, named *lymph-hearts*, and it has been shown that the caudal heart of the eel is a lymph-heart also. The number and positions of these organs vary. In frogs and toads, there are usually four, two anterior and two posterior. Into each of these cavities several lymphatics open, the orifices of the vessels being guarded by valves, which prevent the retrograde passage of the lymph. From each heart a single vessel proceeds, and conveys the lymph directly into the venous system. Blood is prevented from passing into the lymphatic heart by a valve at its orifice.

The muscular coat of these hearts is of variable thickness; in some cases it can only be discovered by means of the microscope; but in every case it is composed of striped fibres. The contractions of the hearts are rhythmical, occurring about sixty times in a minute. The pulsations of the cervical pair are not always synchronous with those of the pair in the ischiatic region, and even the corresponding sacs of opposite sides are not always synchronous in their action.

Unlike the contractions of the blood-heart, those of the lymph-heart appear to be directly dependent upon a certain limited portion of the spinal cord. For Volkmann found that so long as the portion of spinal cord corresponding to the third vertebra of the frog was uninjured, the cervical pair of lymphatic hearts continued pulsating after all the rest of the spinal cord and the brain were destroyed; while destruction of this portion, even though all other parts of the nervous centres were uninjured, instantly arrested the hearts' movements. The posterior, or ischiatic, pair of lymph-hearts were found to be governed, in like manner, by the portion of spinal cord corresponding to the eighth vertebra. Division of the posterior spinal roots did not arrest the movements; but division of the anterior roots caused them to cease at once.

Innervation of the Thoracic Duct.—By determining the rate of outflow of a fluid at constant pressure passing through the thoracic duct, Camus and Gley have obtained evidence of the presence of nerves, causing both dilatation and constriction of the duct. These are contained in the sympathetic chain below the first thoracic ganglion. The effect of stimulation is principally dilatation.

Relation of Lymph and Blood.

The volume of blood in the body remains remarkably constant. If the amount is increased by injection of fluids, at first its specific gravity is lessened, but in a short time, often in a few minutes, it returns to the normal. The excess of fluid is got rid of in two ways: (1) by the kidneys, which secrete profusely; and (2) by the tissues, which become more watery in consequence. After the renal arteries are ligatured, and the kidney is consequently thrown out of action, the excess of water passes only into the tissues.

On the other hand, a deficiency of blood (for instance, after hæmorrhage) is soon remedied by a transfer of water from the tissues to the blood through the intermediation of the lymph.

In severe hæmorrhage life has often been saved by injection of saline solution into the vessels, or by transfusion from another person. The transfer of the blood of another animal to the human vascular system is usually dangerous, especially if the blood has been defibrinated, for the serum of one animal is usually poisonous to another, producing various changes, of which a breakdown of the corpuscles (hæmolysis) is the most constant sign.

Formation of Lymph.

Carl Ludwig taught that the lymph flow is conditioned by two factors: first, differences in the pressure of the blood in the capillaries and of the fluid in the tissue spaces, giving rise to a *filtration* of fluid through the capillary walls; and secondly, chemical differences between these two fluids, setting up *osmotic* interchanges through the wall of the blood-vessel.

The accurate meaning of these terms is explained in the section in small print at the end of this chapter.

If the lymph is produced by a simple act of filtration, then the amount of lymph must rise and sink with the value of D—*d*; D representing the capillary blood-pressure, and *d* the pressure in the tissue spaces.

In support of this mechanical theory, various workers in Ludwig's laboratory showed that increased capillary pressure due to obstruction of the venous outflow increases the amount of lymph formed; and that diminution of the pressure in the lymph spaces, by squeezing out the lymph previously contained in them, leads to an increase in the transudation.

On the other hand, there were some facts which could not be well explained by the filtration theory, among which may be mentioned the action of curare in causing an increase of lymph flow.

Heidenhain was the first to fully recognise that the laws of filtration and osmosis as applied to dead membranes may be considerably modified when the membranes are composed of living cells; and he considered that the formation of lymph is due to the selective or secretory activity of the endothelial walls of the capillaries. This so-called vital action of the endothelial cells is seen in the fact that after the injection of sugar into the blood, in a short time the percentage of sugar in the lymph becomes higher than that in the blood. There must, therefore, be some activity of the endothelial cells in picking out the sugar from the blood and passing it on to the lymph.

Heidenhain is also the inventor of the term *lymphagogues* (literally, lymph drivers). These are substances like curare, which have a specific action in causing an increased lymph flow. Heidenhain considers the majority of these act by stimulating the endothelial cells to activity. This conclusion, however, has been subjected to much criticism. In this country the question has been taken up by Starling, who has shown that the influence of vital action is not so marked as Heidenhain supposes it to be, but that most of the phenomena in connection with lymph formation can be explained by the simpler mechanical theory. Starling's views may be briefly stated as follows:—

The amount of lymph produced in any part depends on two factors:—

1. The pressure at which the blood is flowing through the capillaries. Heidenhain took the arterial pressure in his experiments as the measure of the capillary pressure; Starling points out, very

justly, that this is incorrect, as there is between the arteries and the capillaries the peripheral resistance in the arterioles.

2. The permeability of the capillary wall. This varies enormously in different regions; it is greatest in the liver, so that an intracapillary pressure which would cause lymph to flow here is without effect on the production of lymph in the limbs.

The flow of lymph may therefore be increased in two ways:—

1. By increasing the intracapillary pressure. This may be done locally by ligaturing the veins of an organ; or generally by injecting a large amount of fluid into the circulation, or by the injection of such substances as sugar and salt (Heidenhain's first class of lymphagogues) into the blood. These attract water from the tissues into the blood, and thus increase the volume of the circulating fluid and raise the intracapillary pressure.

2. By increasing the permeability of the capillary wall by injuring its vitality. This may be done locally by scalding a part; or generally, by injecting certain poisonous substances, such as peptone, leech extract, decoction of mussels, etc. (Heidenhain's second class of lymphagogues). These act chiefly on the liver capillaries; curare acts chiefly on the limb capillaries.

In the light of our present knowledge on this question, it is impossible to pronounce any absolutely positive opinion. But facts appear to me to be accumulating which tell in favour of the secretion theory. If the endothelial wall were a non-living membrane, physical processes would obviously explain all the phenomena of lymph formation. But we must recognise that the endothelial cells are alive, and that like other cells they are capable of a selective action which may mask or counteract or assist the purely physical processes. If the action of poisons was simply to injure the vessel wall and increase its permeability, the amount of lymph should be proportional to the intensity of the injury; but this is not found to be the case. Heidenhain no doubt went too far when he attributed lymph formation almost exclusively to endothelial activity; and Starling has gone too far in the other direction. My own opinion is that lymph formation is mainly influenced by the physical conditions present, for the action of such thin cells as those of the capillary wall cannot be sufficiently great to entirely counteract these conditions; at the same time it is impossible to deny that there is some such action as may be described by the terms "selective" or "secretory." The question is closely related to that of absorption from the alimentary canal, and we shall find in studying that subject that there is a similar difference of opinion, and that recently published researches confirm the theory of selective activity of the absorptive epithelium.

Osmotic Phenomena.

The investigations of physical chemists during recent years have given us new conceptions of the nature of solutions, and these have important bearings on the explanation of osmotic phenomena, and so are interesting to the physiologist.

Water is the fluid in which soluble materials are usually dissolved, and at ordinary temperatures it is a fluid the molecules of which are in constant movement; the hotter the water the more active are the movements of its molecules, until when at last it is converted into steam, the molecular movements become much more energetic. Perfectly pure water consists of molecules with the formula H_2O, and these molecules undergo practically no dissociation into their constituent ions, and it is for this reason that pure water is not a conductor of electricity.

If a substance like sugar is dissolved in the water, the solution still remains incapable of conducting an electrical current. The sugar molecules in solution are still sugar molecules; they do not undergo dissociation.

But if a substance like salt is dissolved in the water, the solution is then capable of conducting electrical currents, and the same is true for most acids, bases, and salts. These substances do undergo dissociation, and the simpler materials into which they are broken up in the water are called *ions*. Thus, if sodium chloride is dissolved in water a certain number of its molecules become dissociated into sodium ions, which are charged positively with electricity, and chlorine ions, which are charged negatively with electricity. Similarly a solution of hydrochloric acid in water contains free hydrogen ions and free chlorine ions. Sulphuric acid is decomposed into hydrogen ions and ions of SO_4. The term ion is thus not equivalent to atom, for an ion may be a group of atoms, like SO_4, in the example just given.

Further, in the case of hydrochloric acid, the negative charge of the chlorine ion is equal to the positive charge of the hydrogen ion; but in the case of the sulphuric acid, the negative charge of the SO_4 ion is equal to the positive charge of two hydrogen ions. We can thus speak of monovalent, divalent, trivalent, etc., ions.

Ions positively charged are called *kat-ions* because they move towards the kathode or negative pole; those which are negatively charged are called *an-ions* because they move towards the anode or positive pole. The following are some examples of each class:—

Kat-ions. Monovalent:—H, Na, K, NH_4, etc.
Divalent:—Ca, Ba, Fe (in ferrous salts), etc.
Trivalent:—Al, Bi, Sb, Fe (in ferric salts), etc.
An-ions. Monovalent:—Cl, Br, I, OH, NO_3, etc.
Divalent:—S, Se, SO_4, etc.

Roughly speaking, the greater the dilution the more nearly complete is the dissociation, and in a very dilute solution of such a substance as sodium chloride we may consider that the number of ions is double the number of molecules of the salt present.

The ions liberated by the act of dissociation are, as we have seen, charged with electricity, and when an electrical current is led into such a solution, it is conducted through the solution by the movement of the ions. Substances which exhibit the property of dissociation are known as electrolytes.

The liquids of the body contain electrolytes in solution, and it is owing to this fact that they are able to conduct electrical currents.

This conception of electrolytes which we owe to Arrhenius is extremely important in view of the question of osmotic pressure, because the act of dissociation increases the number of particles moving in the solution, and so increases the osmotic pressure, for in this relation an ion plays the same part as a molecule.

Another physiological aspect of the subject is seen in a study of the actions of mineral salts in solution on living organisms and parts of organisms. Many years ago Ringer showed that contractile tissues (heart, cilia, etc.) continue to manifest their activity in certain saline solutions. We have already seen (p. 256) that Howell considers the cause of rhythmical action in the heart is the presence of these inorganic substances in the blood or lymph which bathes it.

Loeb and his fellow-workers have confirmed these statements, but interpret them now as ionic action. Contractile tissues will not contract in pure solutions of non-electrolytes (like sugar, urea, albumin). But different contractile tissues differ in the nature of the ions which are most favourable stimuli. Thus cardiac muscle, cilia, amœboid movement, karyokinesis, cell division, are all alike in requiring a proper adjustment of ions in their surroundings if they are to continue to act, but the proportions must be different in individual cases. Ions affecting the rhythmical contractions may be divided into three classes: (1) Those which produce such contractions; of these the most efficacious is Na. (2) Those which retard or inhibit rhythmical contractions; for instance, Ca and K. (3) Those which act catalytically, that is, they accelerate the action of Na, though they do not themselves produce rhythmical contractions directly: for instance, H and OH. In spite of the antagonistic effect of Ca, a certain minimal amount of it must be present if contractions are to continue for any length of time. Ions produce rhythmical contraction only because they affect either the physical condition of the colloidal substances (proteid, etc.) in protoplasm, or the rapidity of chemical processes.

Loeb has even gone so far as to consider that the process of fertilisation is mainly ionic action. He denies that the nuclein in the head of the spermatozoon is essential, but asserts that all the spermatozoon does is to act as the stimulus in the due adjustment of the proportions of the surrounding ions. He supports this view by numerous experiments on ova, in which, without the presence of spermatozoa, he has produced larvæ (generally imperfect ones, it is true) by merely altering the saline constituents of the fluid that bathes them. Whether such a sweeping and almost revolutionary notion will stand the test of further verification must be left to the future. So also must the equally important idea that the basis of a nerve-impulse is electrolytic action.

Gramme-molecular Solutions.—From the point of view of osmotic pressure a convenient unit is the gramme-molecule. A gramme-molecule of any substance is the quantity in grammes of that substance equal to its molecular weight. A gramme-molecular solution is one which contains a gramme-molecule of the substance per litre. Thus a gramme-molecular solution of sodium chloride is one which contains 58·5 grammes of sodium chloride ($Na=23{\cdot}05$; $Cl=35{\cdot}45$) in a litre. A gramme-molecular solution of grape sugar ($C_6H_{12}O_6$) is one which contains 179·58 grammes of grape sugar in a litre. A gramme-molecule of hydrogen (H_2) is 2 grammes by weight of hydrogen, and if this was compressed to the volume of a litre, it would be comparable to a gramme-molecular solution. It therefore follows that a litre containing 2 grammes of hydrogen contains the same number of molecules of hydrogen in it as a litre of a solution containing 58·5 grammes of sodium chloride, or one containing 179·58 grammes of grape sugar, has in it of salt or sugar molecules respectively. To put it another way, the heavier the weight of a molecule of any substance, the more of that substance must be dissolved in the litre to obtain its gramme-molecular solution. Or still another way: if solutions of various substances are made all of the same strength per cent., the solutions of the materials of small molecular weight will contain more molecules of those materials than the solutions of the materials which have heavy molecules. We shall see that the calculation of osmotic pressure depends upon these facts.

Diffusion, Dialysis, Osmosis.—If two gases are brought together within a closed space, a homogeneous mixture of the two is soon obtained. This is due to the movements of the gaseous molecules within the confining space, and the process is called *diffusion*. In a similar way diffusion will effect in time a homogeneous mixture of two liquids or solutions. If water is carefully poured on to the surface of a solution of salt, the salt or its ions will soon be equally distributed throughout the whole. If a solution of albumin or any other *colloidal* substance is used instead of salt in the experiment, diffusion will be found to occur much more slowly. If, instead of pouring the water on to the surface of a solution of salt or sugar, the two are separated by a membrane made of such a material as parchment paper, a similar diffusion will occur, though more slowly than in cases where the membrane is absent. In time, the water on each side of the membrane will contain the same quantity of sugar or salt. Substances which pass through such membranes are called *crystalloids*. Substances which have such large molecules (starch, proteid, etc.) that they will not pass through such membranes are called *colloids*. Diffusion of substances in solution which have to deal with an intervening membrane is usually called *dialysis*. The process of *filtration* (*i.e.*, the passage of materials through the pores of a membrane under the influence of mechanical pressure) may be excluded in such experiments by placing the membrane (M) vertically as shown in the diagram (fig. 307), and the two fluids A and B on each side of it. Diffusion through a membrane is not limited to the molecules of water, but it may occur also in the molecules of certain substances dissolved in the water. But very few or no membranes are equally permeable to water and to molecules of the substances dissolved in the water. If in the accompanying diagram the compartment A is filled with pure water, and B with a sodium chloride solution, the liquids in the two compartments will ultimately be found to be equal in bulk as they were at the start, and each will be a solution of salt of half the original strength of that in the compartment B. But at first the volume of the liquid in compartment B increases, because more water molecules pass into it from A than salt molecules pass from B to A. The term *osmosis* is generally limited to the stream of water molecules passing through a membrane, while the term *dialysis* is applied to the passage of the molecules in solution in the water. The osmotic stream of water is especially important, and in connection with this it is necessary to explain the term *osmotic pressure*. At first, then, osmosis (the diffusion of water) is more rapid than the dialysis (the diffusion of the salt molecules or ions). The older explanation of this was that salt attracted the water, but we now express the fact differently by saying that the salt in solution exerts a certain osmotic pressure: the result of the osmotic pressure is that more water flows from the water side to the side of the solution than in the contrary direction. The osmotic pressure varies with the amount of substance in solution, and is also altered by variations of temperature occurring more rapidly at high than at low temperatures.

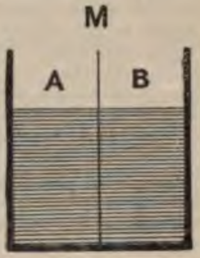


Fig. 307.

If we imagine two masses of water separated by a permeable membrane, as many water molecules will pass through from one side as from the other, and so the volumes of the two masses of water will remain unchanged. If now we imagine the membrane M is not permeable except to water, and the compartment A contains water, and the compartment B contains a solution of salt or sugar; under these circumstances water will pass through into B, and the volume of B will increase in proportion to the osmotic pressure of the sugar or salt in solution in B, but no molecules of sugar or salt can get through into A from B, so the volume of fluid in A will continue to decrease, until at last a limit is reached. The determination of this limit, as measured by the height of a column of fluid or mercury which it will support, will give us a measurement of the osmotic pressure.

If a bladder containing strong salt solution is placed in a vessel of distilled water, water passes into the bladder by osmosis, so that the bladder is swollen, and a manometer connected with its interior will show a rise of pressure (osmotic pressure). But the total rise of pressure cannot be measured in this way for two reasons: (1) because the salt diffuses out as the water diffuses in; and (2) because the membrane of the bladder leaks; that is, permits of filtration when the pressure within it has attained a certain height.

It is therefore necessary to use a membrane which will not allow salt to pass out either by dialysis or filtration, though it will let the water pass in. Such membranes are called *semipermeable* membranes, and one of the best of these is ferrocyanide of copper. This may be made by taking a cell of porous earthenware and washing it out first with copper sulphate and then with potassium ferrocyanide. An insoluble precipitate of copper ferrocyanide is thus deposited in the pores of the earthenware.

If such a cell is arranged as in fig. 308, and filled with a 1 per cent. solution of sodium chloride, water diffuses in, till the pressure registered by the manometer reaches the enormous height of 5000 mm. of mercury. If the pressure in the cell is increased beyond this artificially, water will be pressed through the semi-permeable walls of the cell and the solution will become more concentrated.

In other words, in order to make a solution of sodium chloride of greater concentration than 1 per cent., a pressure greater than 5000 mm. of mercury must be employed. The osmotic pressure exerted by a 2 per cent. solution would be twice as great.

Though it is theoretically possible to measure osmotic pressure by a manometer in this direct way, practically it is hardly ever done, and some of the indirect methods of measurement described later are used instead. The reason for this is that it has been found impossible to construct a membrane which is absolutely semi-permeable; they are all permeable in some degree to the molecules of the dissolved crystalloid. In course of time, therefore, the dissolved crystalloid will be equally distributed on both sides of the membrane, and osmosis of water will cease to be apparent, since it will be equal in both directions.

Many explanations of the nature of osmotic pressure have been brought forward, but none is perfectly satisfactory. The following simple explanation is perhaps the best, and may be rendered most intelligible by an illustration. Suppose we have a solution of sugar separated by a semi-permeable membrane from water; that is, the membrane is permeable to water molecules, but not to sugar molecules. The streams of water from the two sides will then be unequal; on one side we have water molecules striking against the membrane in what we may call normal numbers, while on the other side both water molecules and sugar molecules are striking against it. On this side, therefore, the sugar molecules take up a certain amount of room, and do not allow the water molecules to get to the membrane; the membrane is, as it were, screened against the water by the sugar, therefore fewer water molecules will get through from the screened to the unscreened side than *vice versâ*. This comes to the same thing as saying that the osmotic stream of water is greater from the unscreened water side to the screened sugar side than it is in the reverse direction. The more sugar molecules that are present, the greater will be their screening action, and thus we see that the osmotic pressure is proportional to the number of sugar molecules in the solution, that is, to the concentration of the solution.

Osmotic pressure is, in fact, equal to that which the dissolved substance would exert if it occupied the same space in the form of a gas (Van't Hoff's hypothesis). The nature of the substance makes no difference; it is only the number of molecules which causes osmotic pressure to vary. The osmotic pressure, however, of substances like sodium chloride, which are electrolytes, is greater than what one would expect from the number of molecules present. This is because the molecules in solution are split into their constituent ions, and an ion plays the same part as a molecule, in questions of osmotic pressure. In dilute solutions of sodium chloride ionisation is more complete, and as the total number of ions is then nearly double the number of original molecules, the osmotic pressure is nearly double what would have been calculated from the number of molecules.

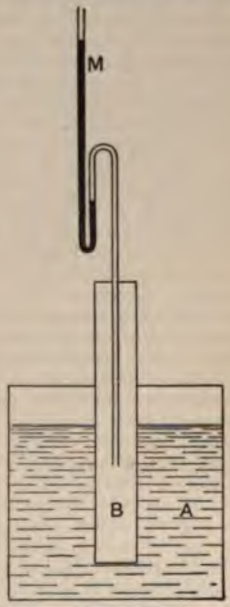


FIG. 308.—A, outer vessel, containing distilled water; B, inner semi-permeable vessel, containing 1 per cent. salt solution; M, mercurial manometer. (After Starling.)

The analogy between osmotic pressure and the pressure of gases is very complete, as may be seen from the following statements :—

1. At a constant temperature osmotic pressure is proportional to the concentration of the solution (Boyle-Mariotte's law for gases).

2. With constant concentration, the osmotic pressure rises with and is proportional to the temperature (Gay-Lussac's law for gases).

3. The osmotic pressure of a solution of different substances is equal to the sum of the pressures which the individual substances would exert if they were alone in the solution (Henry-Dalton law for partial pressure of gases).

4. The osmotic pressure is independent of the nature of the substance in solution, and depends only on the number of molecules or ions in solution (Avogadro's law for gases).

Calculation of Osmotic Pressure.—We may best illustrate this by an example, and to simplify matters we will take an example in the case of a non-electrolyte like sugar. We shall then not have to take into account any electrolytic dissociation of the molecules into ions. We will suppose we want to calculate the osmotic pressure of a 1 per cent. solution of cane sugar.

One gramme of hydrogen at atmospheric pressure and 0° C. occupies a volume of 11·19 litres; two grammes of hydrogen will therefore occupy a volume of 22·38 litres. A gramme-molecule of hydrogen—that is, 2 grammes of hydrogen—when brought to the volume of 1 litre, will exert a gas pressure equal to that of 22·38 litres compressed to 1 litre—that is, a pressure of 22·38 atmospheres. A gramme-molecular solution of cane sugar, since it contains the same number of molecules in a litre, must therefore exert an osmotic pressure of 22·38 atmospheres also. A gramme-molecular solution of cane sugar ($C_{12}H_{22}O_{11}$) contains 342 grammes of cane sugar in a litre. A 1 per cent. solution of cane sugar contains only 10 grammes of cane sugar in a litre; hence the osmotic pressure of a 1 per cent. solution of cane sugar is $\frac{10}{342} \times 22{\cdot}38$ atmospheres, or 0·65 of an atmosphere, which in terms of a column of mercury = 760 × 0·65 = 494 mm.

It would not be possible to make such a calculation in the case of an electrolyte, because we should not know how many molecules had been ionised. In the liquids of the body, both electrolytes and non-electrolytes are present, and so a calculation is here also impossible.

We have seen that for such liquids the osmotic pressure cannot be directly measured by a manometer, because there are no perfect semi-permeable membranes; we now see that mere arithmetic often fails us; and so we come to the question to which we have been so long leading up, viz., how osmotic pressure is actually determined.

Determination of Osmotic Pressure by means of the Freezing-point.—This is the method which is almost universally employed. A very simple apparatus (Beckmann's differential thermometer) is all that is necessary. The principle on which the method depends is the following:—The freezing-point of any substance in solution in water is lower than that of water; the lowering of the freezing-point is proportional to the molecular concentration of the dissolved substance, and that, as we have seen, is proportional to the osmotic pressure.

When a gramme-molecule of any substance is dissolved in a litre of water, the freezing-point is lowered by 1·87° C., and the osmotic pressure is, as we have seen, equal to 22·38 atmospheres, that is, 22·38 × 760 = 17,008 mm. of mercury.

We can, therefore, calculate the osmotic pressure of any solution if we know the lowering of its freezing-point in degrees Centigrade; the lowering of the freezing-point is usually expressed by the Greek letter Δ.

$$\text{Osmotic pressure} = \frac{\Delta}{1{\cdot}87} \times 17{,}008.$$

For example, a 1 per cent. solution of sugar would freeze at $-0{\cdot}052^\circ$ C.; its osmotic pressure is therefore $\frac{{\cdot}052 \times 17{,}008}{1{\cdot}87} = 473$ mm., a number approximately equal to that we obtained by calculation.

Mammalian blood serum gives $\Delta = 0{\cdot}56^\circ$ C. A 0·9 per cent. solution of sodium chloride has the same Δ; hence serum and a 0·9 per cent. solution of common salt have the same osmotic pressure, or are *isotonic*. The osmotic pressure of blood serum is $\frac{{\cdot}56 \times 17{,}008}{1{\cdot}87} = 4987$ mm. of mercury, or a pressure of nearly 7 atmospheres.

The osmotic pressure of solutions may also be compared by observing their effect on red blood corpuscles, or on vegetable cells such as those in Tradescantia. If the solution is *hypertonic*, *i.e.*, has a greater osmotic pressure than the cell contents, the protoplasm shrinks, and loses water, or if red corpuscles are used, they become crenated; if the solution is *hypotonic*, *i.e.*, has a less osmotic pressure than the material within the cell-wall, no shrinking of the protoplasm in the vegetable cell takes place; and if red corpuscles are used they swell and liberate their pigment. *Isotonic* solutions, like physiological salt solution, produce neither of these effects, because they have the same molecular concentration and osmotic pressure as the material within the cell-wall.

Physiological Applications.—It will at once be seen how important all these considerations are from the physiological standpoint. In the body we have aqueous solutions of various substances separated from one another by membranes. Thus we have the endothelial walls of the capillaries separating the blood from the lymph; we have the epithelial walls of the kidney tubules separating the blood and lymph from the urine; we have similar epithelium in all secreting glands; and we have the wall of the alimentary canal separating the digested food from the blood-vessels and lacteals. In such important problems, then, as lymph-formation, the formation of urine and other excretions and secretions, and absorption of food, we have to take into account the laws which regulate the movements both of water and of substances which are held in solution by the water. In the body osmosis is not the only force at work, but we have also to consider filtration, that is, the forcible passage of materials through membranes, due to differences of mechanical pressure. Further complicating these two processes we have to take into account another force, namely, the secretory or selective activity of the living cells of which the membranes in question are composed. This is sometimes called by the name *vital action*, which is an unsatisfactory and unscientific expression. The laws which regulate filtration, inhibition, and osmosis are fairly well known and can be experimentally verified. But we have undoubtedly some other force, or some other manifestation of force, in the case of living membranes. It probably is some physical or chemical property of living matter which has not yet been brought into line with the known chemical and physical forces which operate in the inorganic world. We cannot deny its existence, for it sometimes operates so as to neutralise the known forces of osmosis and filtration.

The more one studies the question of lymph-formation, the more convinced one becomes that mere osmosis and filtration will not explain it entirely. The basis of the action is no doubt physical, but the living cells do not behave like the dead membranes of a dialyser; they have a selective action, picking out some substances and passing them through to the lymph, while they reject others.

The question of gaseous interchanges in the lungs is another of a similar kind. Some maintain that all can be explained by the laws of diffusion of gases; others assert that the action is wholly vital. Probably those are most correct who admit a certain amount of truth in both views; the main facts are explicable on a physical basis, but there are also some puzzling data that show that the pulmonary epithelium is able to exercise some other force as well which interferes to some extent with the known physical process. Take again the case of absorption. The object of digestion is to render the food soluble and diffusible; it can hardly be supposed that this is useless; the readily diffusible substances will pass more easily through into the blood and lymph: but still, as Waymouth Reid has shown, if the living epithelium of the intestine is removed, absorption comes very nearly to a standstill, although from the purely physical standpoint removal of the thick columnar epithelium would increase the facilities for osmosis and filtration.

The osmotic pressure exerted by crystalloids is very considerable, but their ready diffusibility limits their influence on the flow of water in the body. Thus if a strong solution of salt is injected into the blood, the first effect will be the setting up of an osmotic stream from the tissues to the blood. The salt, however, would soon diffuse out into the tissues, and would now exert osmotic pressure in the opposite direction. Moreover, both effects will be but temporary, because excess of salt is soon got rid of by the excreting organs.

Osmotic Pressure of Proteids.—It has been generally assumed that proteids, the most abundant and important constituents of the blood, exert little or no osmotic pressure. Starling, however, has claimed that they have a small osmotic pressure; if this is so, it is of importance, for proteids, unlike salt, do not diffuse readily, and their effect therefore remains as an almost permanent factor in the blood. Starling gives the osmotic pressure of the proteids of the blood-plasma as equal to 30 mm. of mercury. We should from the theoretical standpoint find it difficult to imagine that a pure proteid can exert more than a minimal osmotic pressure. It is made up of such huge molecules that, even when the proteids are present to the extent of 7 or 8 per cent., as they are in blood-plasma, there are comparatively few proteid molecules in solution. Still, by means of this weak but constant pressure it is possible to explain the fact that an isotonic or even a hypertonic solution of a diffusible crystalloid may be completely absorbed from the peritoneal cavity into the blood.

The functional activity of the tissue elements is accompanied by the breaking down of their proteid constituents into such simple materials as urea (and its precursors) sulphates and phosphates. These materials pass into the lymph, and increase its molecular concentration and its osmotic pressure; thus water is attracted (to use the older way of putting it) from the blood to the lymph, and so the volume of the lymph rises and its flow increases. On the other hand, as these substances accumulate in the lymph they will in time attain there a greater concentration than in the blood, and so they will diffuse towards the blood, by which they are carried to the organs of excretion.

But, again, we have a difficulty with the proteids; they are most important for the nutrition of the tissues, but they are practically indiffusible. We must provisionally assume that their presence in the lymph is due to filtration from the blood. The plasma in the capillaries is under a somewhat higher pressure than the lymph in the tissues, and this tends to squeeze the constituents of the blood, including the proteids, through the capillary walls. I have, however, already indicated that the question of lymph-formation is one of the many physiological problems which await solution by the physiologists of the future.

B. Moore and W. H. Parker confirm Starling's hypotheses that colloids in solution exert a small osmotic pressure, but the direct method is the only one available to determine it, the variations in freezing or boiling points are too small. It was hoped that this pressure could be used for determining the molecular weight of colloids like proteids, but it is found that in the case of substances of known molecular weight such as soaps, the apparent molecular weights are from 20 to 60 times too large. There must thus be a physical union or association of molecules to form a single osmotic unit. It is, therefore, possible that the chemical molecule of a proteid is not so large as has been supposed, but its apparent size is due to a physical aggregation of many molecules. Moore doubts whether the differences in osmotic pressure are sufficiently great to explain absorption, lymph production, or the formation of urine. If this is so, the *physiological* factor, the so-called vital activity of the cells, must be called in to explain these phenomena.

Waymouth Reid finds that absolutely pure proteids exert no osmotic pressure; the pressure observed is due to saline and other materials from which it is difficult to disentangle the proteid.

Dr C. J. Martin has suggested to me a way of illustrating the so-called selective action of living membranes. Suppose a number of fishes are swimming about in a tank, like moving molecules or ions in solution; across the tank is a wall which divides it into two parts; the fishes are all in one compartment of the tank. Suppose, next, the wall has in it a number of holes guarded by valves, so arranged that the fish can pass through into the second compartment, but cannot return. After a time, as the fish discover these holes, there will be an equal number of fish in both compartments; but this is not the end, for on waiting further, more fish will find their way through, and as none are able to return, they will all in time accumulate in the second compartment. It is not difficult to grasp the idea that the arrangement of molecules in a living membrane is possibly such that the orifices through which other molecules pass are valvular, and such a conception is useful if it merely serves to rob the word "vital" of its mystery.

CHAPTER XXIII

THE DUCTLESS GLANDS

THE ductless glands form a heterogeneous group of organs, most of which are related in function or development with the circulatory system. They include the lymphatic glands, the spleen, the thymus, the thyroid, the suprarenal capsules, the pineal body, the pituitary body, and the carotid and coccygeal glands. The function of a gland that has a duct is a comparatively simple physiological problem, but the use of ductless glands has long been a puzzle to investigators. Recent research has, however, shown that most of, if not all, the ductless glands do form a secretion, and this *internal secretion*, as it is termed, leaves the gland by the venous blood or lymph, and thus is distributed and ministers to the needs of parts of the body elsewhere. Many of the glands which possess ducts and form an external secretion, form an internal secretion as well. Among these, the liver, pancreas, and kidney may be mentioned.

In many cases the internal secretion is essential for life, and removal of the gland that forms it, leads to a condition of disease culminating in death. In other cases the internal secretion is not essential, or its place is taken by that formed in similar glands in other parts of the body.

The body is a complex machine; each part of the machine has its own work to do, but must work harmoniously with other parts. Just as a watch will stop if any of its numerous wheels get broken, so the metabolic cycle will become disarranged or cease altogether if any of the links in the chain break down.

In unravelling the part which the ductless glands play in this cycle, it is at present impossible in many cases to state precisely what the particular function of each is; all one can say is, when the gland is removed or its function interfered with, that the metabolic round is broken somehow, and that this upsets the whole of the machinery of the body. The difficulty of investigating this subject is increased by the fact that it is impossible to get the internal secretion in a state of purity and examine it; it is always mixed with, and masked by, the lymph or blood into which it is poured.

In spite of this, however, our knowledge in this branch of physiology is increasing, particularly in connection with some of these ductless glands. The methods of investigation which have been employed are the following:—

1. *Extirpation.*—The gland in question is removed, and the effect of the absence of the internal secretion noted.

2. *Disease.*—In cases where the function of the gland is in abeyance, owing to its being diseased, the symptoms are closely observed.

3. *Injection of Extracts.*—The gland is taken in a fresh condition; an extract is made of it, and this is injected into the circulation of healthy animals, and into that of those animals from which the gland has been previously removed, and the effects watched.

4. *Transplantation.*—After the gland is removed and the usual effect produced, the same gland from another animal is transplanted into the first animal, and restoration of function looked for.

The case of the lymphatic glands we have already studied; they form an internal secretion which consists of lymph-cells, and these furnish the blood with its most important supply of colourless corpuscles. Removal of lymphatic glands is not fatal, as the other lymphatic glands and other collections of lymphoid tissue that remain behind carry on the work of those that are removed.

The internal secretion theory of the ductless glands is that which is most in vogue at present. It should be mentioned, however, that there is another theory, which may be called the *auto-intoxication* theory. According to this view the gland is excretory (*i.e.*, gets rid of waste and harmful materials) rather than secretory (*i.e.*, production of something useful to the organism). When the gland is removed, the waste products therefore accumulate and produce harmful results. It is possible that as our knowledge increases, it may be found in certain cases that both these theories may be in part true.

The Spleen.

The Spleen is the largest of the ductless glands; it is situated to the left of the stomach, between it and the diaphragm. It is of a deep red colour and of variable shape. Vessels enter and leave the gland at a depression on the inner side called the *hilus.* The spleen is covered externally almost completely by a serous coat derived from the peritoneum, while within this is the proper fibrous coat or capsule of the organ. The latter is composed of connective-tissue, with a large preponderance of elastic fibres and a certain proportion of unstriated muscular tissue. Prolonged from its inner surface are fibrous processes or *trabeculæ,* containing much unstriated muscle, which enter the interior of the organ, and, dividing and anastomosing in all parts, form a supporting framework in the interstices of which the proper substance of the spleen (*spleen-pulp*) is contained.

At the hilus of the spleen, the blood-vessels, nerves, and lymphatics enter or leave, and the fibrous coat is prolonged into the spleen substance in the form of investing sheaths for the arteries and veins, which sheaths again are continuous with the trabeculæ before referred to.

The *spleen-pulp*, which is of a dark red or reddish-brown colour, is composed chiefly of cells, imbedded in a network formed of fibres, and the branchings of large nucleated cells. The network so formed is thus very like a coarse kind of retiform tissue. The spaces of this network are only partially occupied by cells and form a freely communicating system. Of the cells some are granular corpuscles resembling the lymph-corpuscles, both in general appearance and in being able to perform amœboid movements; others are red blood-corpuscles of normal appearance or variously changed; while there

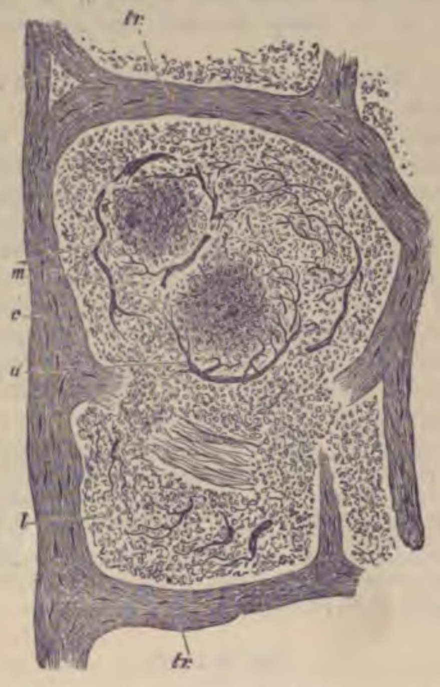


FIG. 309.—Section of injected dog's spleen. *c*, capsule; *tr*, trabeculæ; *m*, two Malpighian bodies with numerous small arteries and capillaries; *a*, artery; *l*, lymphoid tissue, consisting of closely-packed lymphoid cells supported by very delicate retiform tissue; a light space unoccupied by cells is seen all round the trabeculæ, which corresponds to the "lymph-path" in lymphatic glands. (Schofield.)

are also large cells containing either a pigment allied to the colouring matter of the blood, or rounded corpuscles like red corpuscles.

The splenic artery, after entering the spleen by its concave surface, divides and subdivides, with but little anastomosis between its branches; at the same time its branches are sheathed by the prolongations of the fibrous coat, which they, so to speak, carry into the spleen with them. The arteries soon leave the trabeculæ, and their outer coat is then replaced by one of lymphoid tissue; they end in an open brush-work of capillaries, the endothelial cells of which become continuous with those of the *rete* of the spleen-pulp. The veins begin by a similar open set of capillaries from the large blood spaces of the pulp. The veins soon pass into the trabeculæ, and ultimately unite to form the splenic vein. This arrangement readily allows lymphoid and other corpuscles to be swept into the blood-current.

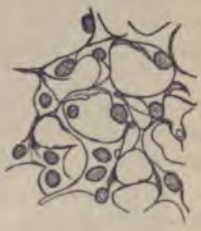


FIG. 310.—Reticulum of the spleen of a cat, shown by injection with gelatine. (Cadiat.)

On the face of a section of the spleen can be usually seen readily with the naked eye, minute, scattered, rounded or oval whitish spots, mostly from $\frac{1}{30}$ to $\frac{1}{60}$ inch ($\frac{5}{6}$ to $\frac{2}{5}$ mm.) in diameter. These are the *Malpighian corpuscles* of the spleen, and are situated on the sheaths of the minute splenic arteries. They are in fact outgrowths of the outer coat of lymphoid tissue just referred to (see fig. 309). Blood capillaries traverse the Malpighian corpuscles and form a plexus in their interior. The structure of a Malpighian corpuscle of the spleen is practically identical with that of a lymphoid nodule.

The spleen has the following functions:—

(1.) The spleen, like the lymphatic glands, is engaged in *the formation of colourless blood-corpuscles.* For it is quite certain, that the blood of the splenic vein contains an unusually large proportion of white corpuscles; and in the disease termed *leucocythæmia,* in which the white corpuscles of the blood are remarkably increased in number, there is found a hypertrophied condition of the spleen, especially of the Malpighian corpuscles. The white corpuscles formed in the spleen also doubtless partly leave that organ by lymphatic vessels.

By stimulating the spleen to contract in a case of splenic leucocythæmia by means of an electric current applied over it through the skin, the number of leucocytes in the blood is almost immediately increased.

Removal of the spleen is not fatal; but after its removal there is an overgrowth of the lymphatic glands to make up for its absence.

(2.) It forms *coloured corpuscles,* at any rate, in some animals; in these animals, cells are found in the spleen similar to those we have described in red marrow, and called *hæmatoblasts.* In these animals, if the spleen is removed, the red marrow hypertrophies.

(3.) There is reason to believe that in the spleen many of the *red corpuscles* of the blood, those probably which have discharged their office and are worn out, *undergo disintegration;* for in the coloured portions of the spleen-pulp an abundance of such corpuscles, in various stages of degeneration, are found, and in those cases of disease in which the destruction of blood-corpuscles is increased (pernicious anæmia) iron accumulates in the spleen as in the liver. It was formerly supposed that the spleen broke down the corpuscles and liberated hæmoglobin, which, passing in the blood of the splenic vein to the liver, was discharged by that organ as bile-pigment. But this is not the case; the disintegration does not proceed so far as to actually liberate hæmoglobin; there is no free hæmoglobin in the blood-plasma of the splenic vein.

(4.) From the almost constant presence of uric acid, in larger quantities than in other organs, as well as of the nitrogenous bodies, xanthine and hypoxanthine, in the spleen, some share in *nitrogenous metabolism* may be fairly inferred to occur in it.

(5.) Besides these direct offices, the spleen fulfils some purpose in regard to the portal circulation with which it is in close connection. From the readiness with which it admits of being distended, and from the fact that it is generally small while gastric digestion is going on, and enlarges when that act is concluded, it is supposed to act as a kind of vascular reservoir, or diverticulum to the portal system, or more particularly to the vessels of the stomach. That it may serve such purpose is also made probable by the enlargement which it undergoes in certain affections of the heart and liver, attended with obstruction to the passage of blood through the latter organ, and by its diminution when the congestion of the portal system is relieved by discharges from the bowels, or by the effusion of blood into the stomach. This mechanical influence on the circulation, however, can hardly be supposed to be more than a very subordinate function.

Influence of the Nervous System upon the Spleen.—When the spleen is enlarged after digestion, its enlargement is due to two causes: (1) a relaxation of the muscular tissue which forms so large a part of its framework; (2) a dilatation of the vessels. Both these phenomena are under control of the nervous system. It has been found by experiment that when the splenic nerves are cut the spleen enlarges, and that contraction can be brought about by stimulation of the peripheral ends of the divided nerves. If the splenic nerves are not cut, contraction is produced by (1) stimulation of the spinal cord; (2) reflexly by stimulation of the central stumps of certain divided nerves, *e.g.*, vagus and sciatic; (3) by local stimulation by an electric current; (4) by the administration of quinine and some other drugs.

It has been shown by the oncometer (see p. 308) that the spleen undergoes rhythmical contractions and dilatations, due to the contraction and relaxation of the muscular tissue in its capsule and trabeculæ. A tracing also shows waves due to the rhythmical alterations of the general blood-pressure. Fig. 311 is a typical tracing obtained by Schäfer's air oncometer from a dog's spleen.

It shows, first, the large waves occurring about once a minute, due to the splenic systole and diastole; secondly, smaller waves on this, due to the effect of respiration on the blood-pressure; and on these, smaller waves still, corresponding with the individual heart-beats. The large waves due to the splenic contractility still go on after the division of all the splenic nerves. These nerve-fibres leave the spinal cord in numerous thoracic anterior roots; they have cell stations in the sympathetic chain (Schäfer) or semi-lunar ganglia (Langley).

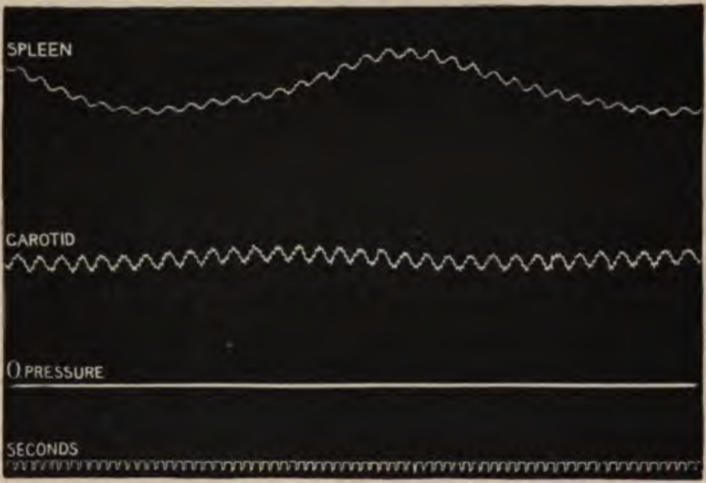


FIG. 311.—The upper tracing is the spleen record; the next is carotid blood-pressure taken with a mercurial kymograph. The straight line beneath this is the abscissa of the arterial pressure; and the lowest tracing is the time in seconds.

Hæmolymph Glands.

The existence of glands which partake of the nature of the spleen, and of lymphatic glands, has long been known. They have been recently more fully investigated by T. Lewis. He finds them in most mammals, and they can be readily distinguished from ordinary lymphatic glands by their red colour. He divides them into (1) *hæmal glands*, which are characterised by the fact that the sinuses contain blood only. The spleen is in fact a large hæmal gland; and (2) *hæmal lymphatic glands*, in which the sinuses are filled by a mixture of blood and lymph.

The Thymus.

This gland is a temporary organ; it attains its greatest size early after birth, and after the second year gradually diminishes, until in adult life hardly a vestige remains. At its greatest development is a long narrow body, situated in the front of the chest behind the sternum and partly in the lower part of the neck. It is of a reddish or greyish colour, and is distinctly lobulated.

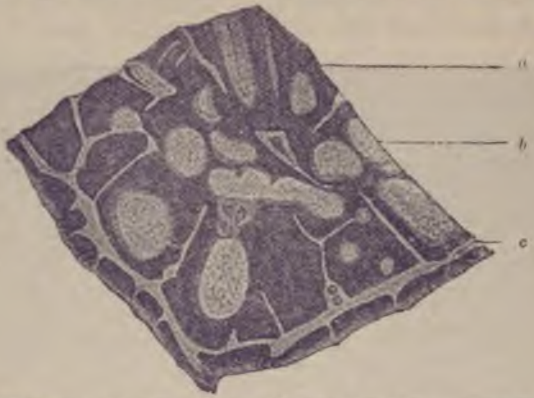


FIG. 312.—Thymus of a calf. *a*, cortex of follicle; *b*, medulla; *c*, interfollicular tissue. Magnified about twelve times. (Watney.)

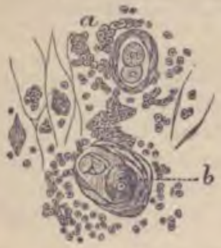


FIG. 313.—The reticulum of the thymus. *a*, lymph cells; *b*, corpuscles of Hassall. (Cadiat.)

The gland is surrounded by a fibrous capsule, which sends in processes, forming trabeculæ, that divide the gland into lobes, and carry the blood- and lymph-vessels. The large trabeculæ branch into small ones, which divide the lobes into lobules. The lobules are further subdivided into follicles by fine connective-tissue. A follicle is polyhedral in shape, and consists of cortical and medullary portions, both of which are composed of adenoid or lymphoid tissue, but in the medullary portion the matrix is coarser, and is not so filled up with lymphoid corpuscles as in the cortex. Scattered in the lymphoid tissue of the medulla are the *concentric corpuscles of Hassall* (fig. 313), which consist of a nucleated granular centre, surrounded by flattened nucleated epithelial cells. These are islands of epithelial cells cut off from the epithelium of the pharynx in process of development. They are not occluded blood-vessels, as was at one time supposed. They remind one somewhat of the epithelial nests seen in some varieties of cancer.

The arteries radiate from the centre of the gland. Lymph sinuses may be seen occasionally surrounding the periphery of the follicles (Klein). The nerves are very minute.

From the thymus various substances may be extracted, many of them similar to those obtained from the spleen, *e.g.*, xanthine, hypoxanthine, adenine, and leucine.

The main constituent of the cells is proteid, and especially nucleo-proteid. Indeed, the thymus is usually employed as the source of nucleo-proteid when one wishes to inject that substance into the blood-vessels of an animal to produce experimentally intravascular clotting. It is, however, not characteristic of the thymus, but is found in all protoplasm. The method of preparation will be given later (see Coagulation of Blood).

The thymus takes part in producing the colourless corpuscles like other varieties of lymphoid tissue. In hibernating animals it exists throughout life, and as each successive period of hibernation approaches it greatly enlarges and becomes laden with fat. Hence it appears to serve for the storing-up of materials which, being reabsorbed during the inactivity of the hibernating period, may maintain the respiration and the temperature of the body in the reduced state to which they fall during that time. Some observers state that it is also a source of the red blood-corpuscles, at any rate in early life.

Removal of the thymus in the frog (in which animal it persists throughout life) produces muscular weakness, paralysis, and finally death. Intravenous injection of extracts of thymus lowers blood-pressure, though the heart may be somewhat accelerated.

The Thyroid.

The thyroid gland is situated in the neck. It consists of two lobes, one on each side of the trachea, extending upwards to the thyroid cartilage, covering its inferior cornu and part of its body; these lobes are connected across the middle line by a middle lobe or isthmus. It is highly vascular, and varies in size in different individuals.

The gland is encased in a capsule of dense areolar tissue. This sends in strong fibrous trabeculæ, which enclose the thyroid *vesicles*—which are rounded or oblong irregular sacs, consisting of a wall of thin hyaline membrane lined by a single layer of short cylindrical or cubical cells. These vesicles are filled with transparent colloid nucleo-albuminous material. The colloid substance increases with age, and the cavities appear to coalesce. In the interstitial connective-tissue is a round meshed capillary plexus, and a large number of lymphatics. The nerves adhere closely to the vessels.

In the vesicles there are, in addition to the yellowish glassy colloid material, epithelium cells, colourless blood-corpuscles, and also coloured corpuscles undergoing disintegration.

It is difficult to state definitely the function of the thyroid body; it is one of those organs of great importance in the metabolic round; and its removal or disease is followed by general disturbances. It no doubt forms an internal secretion; to this the colloid material mentioned contributes, as it is found in the lymphatic vessels of the organ.

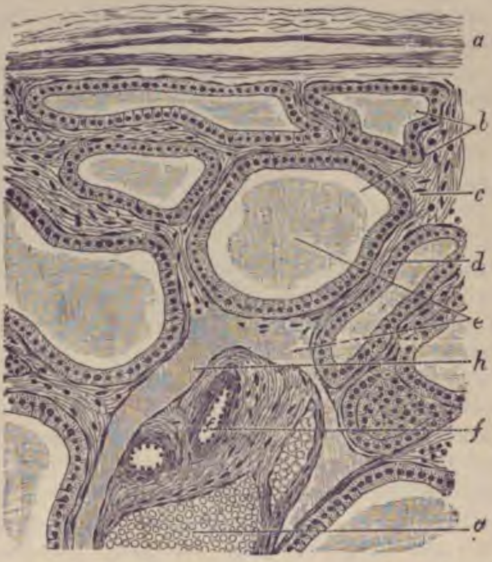


FIG. 314.—Part of a section of the human thyroid. *a*, fibrous capsule; *b*, thyroid vesicles filled with, *e*, colloid substance; *c*, supporting fibrous tissue; *d*, short columnar cells lining vesicles; *f*, arteries; *g*, veins filled with blood; *h*, lymphatic vessels filled with colloid substance. (S. K. Alcock.)

When the gland is diseased in children and its function obliterated, a species of idiocy is produced called *cretinism.*

The same condition in adults is called *myxœdema;* the most marked symptoms of this condition are slowness, both of body and mind, usually associated with tremors and twitchings. There is also a peculiar condition of the skin leading to the overgrowth of the subcutaneous tissues, which in time is replaced by fat; the hair falls off, the hands become spade-like; the whole body is unwieldy and clumsy like the mind.

A similar condition occurs after the thyroid is completely removed surgically; this is called *cachexia strumipriva;* this operation, which was performed previous to our knowledge of the importance of the thyroid, is not regarded as justifiable nowadays.

Lastly, in many animals removal of the thyroid produces analogous symptoms, in the overgrowth of the connective-tissues especially under the skin, and in the nervous symptoms (twitchings, convulsions, etc.).

The term Myxœdema was originally given under the erroneous idea that the swelling of the body is due to mucin. In the early stages of the disease there is a slight increase of mucin, because all new connective-tissues contain a relatively large amount of ground substance, the most abundant constituent of which, next to water, is mucin. But there is nothing characteristic about that.

The discovery of the relationships between the thyroid and these morbid conditions is especially interesting, because important practical results in their treatment have followed close on the heels of experimental investigation. The missing internal secretion of the thyroid may be replaced in these animals and patients by grafting the thyroid of another animal into the abdomen; or more simply by injecting thyroid extract subcutaneously; or even by feeding on the thyroid of other animals. This treatment, which has to be kept up for the rest of the patient's life, is entirely successful. Chemical physiologists have been diligently searching to try and discover what the active material in thyroid extract is which produces such marvellous results; the view at present held is that the efficacy of thyroid extract is due to a substance which Baumann separated from the gland, and which stands almost unique among physiological compounds by containing a large percentage of iodine in its molecule. *Thyro-iodin* or *Iodothyrin*, as this substance has been called, is present in combination with proteid matter in the colloid substance.

Intravenous injection of thyroid extract in a normal animal lowers blood-pressure; but in an animal from which the thyroid has been removed it stimulates the heart and raises blood-pressure.

Parathyroids.

These are small bodies, usually four in number, situated in the neighbourhood of, or embedded in the substance of, the thyroid. They are made up of elongated groups of polyhedral cells, bound together by connective-tissue and well supplied with blood-vessels. Some observers look upon these as being even more essential to healthy life than the thyroid, but this point is by no means decided.

The general idea, however, that prevails is that the thyroid supplies something which is a stimulator of metabolic processes, and that the action on the nervous system is more especially the work of the parathyroids.

The Supra-renal Capsules.

These are two triangular or cocked-hat-shaped bodies, each resting by its lower border upon the upper border of the kidney.

The gland is surrounded by an outer sheath of connective-tissue, which sends in fine prolongations forming the framework of the gland. The gland tissue proper consists of an outside firmer cortical portion and an inside soft, dark medullary portion.

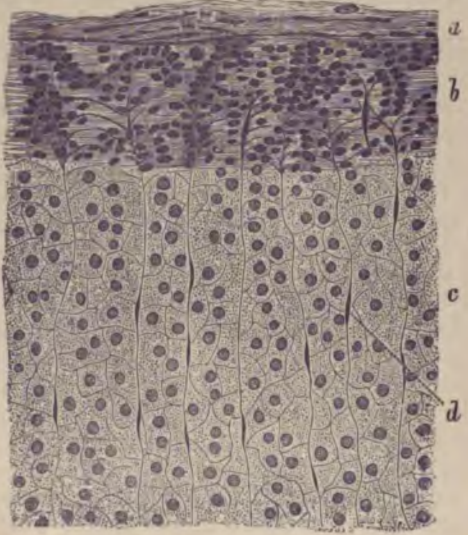


Fig. 315.—Vertical section through part of the cortical portion of supra-renal of guinea-pig. *a*, Capsule; *b*, zona glomerulosa; *c*, zona fasciculata; *d*, connective-tissue supporting the columns of the cells of the latter, and also indicating the position of the blood-vessels. (S. K. Alcock.)

(1.) The *cortical portion* is divided into (fig. 315) columnar groups of cells (*zona fasciculata*). Immediately under the capsule, however, the groups are more rounded (*zona glomerulosa*), while next to the medulla they have a reticular arrangement (*zona reticularis*). The cells themselves are polyhedral, each with a clear round nucleus, and often with oil globules in their protoplasm. The blood-vessels run in the fibrous septa between the columns, but do not penetrate between the cells.

(2.) The *medullary substance* consists of a coarse rounded or irregular meshwork of fibrous tissue, in the alveoli of which are masses of multinucleated protoplasm (fig. 316); numerous blood-vessels; and an abundance of nerve-fibres and cells. The cells are very irregular in shape and size, poor in fat, and often branched; the nerves run through the cortical substance, and anastomose over the medullary portion.

The cells of the medulla are characterised by the presence of certain reducing substances. One of these takes a brown stain with chromic acid, and gives other colour reactions; it is, therefore, called a *chromogen*. Another is similar in many of its characters to jecorin, a lecithin-like substance also found in the liver, spleen, and other organs.

The immense importance of the supra-renal bodies was first indicated by Addison, who, in 1855, pointed out that the disease now known by his name is associated with pathological alterations of these glands. This was tested experimentally by Brown-Séquard, who found a few years later that removal of the supra-renals in animals is invariably and rapidly fatal. The symptoms are practically the same (although more acute) as those of Addison's disease, namely, great muscular weakness, loss of vascular tone, and nervous prostration. The pigmentation (bronzing) of the skin, however, which is a marked symptom in Addison's disease, is not seen in animals. The experiments of Brown-Séquard attracted much attention at the time they were performed, but were almost forgotten until quite recently, when they were confirmed by Abelous, Langlois, Schäfer, and others. The effects on the muscular system are the most marked results both after removal of the capsules and after injection of an extract of the glands. The effect of injecting such an extract on the voluntary

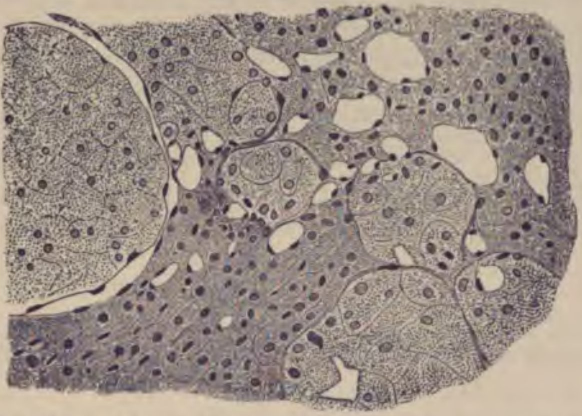
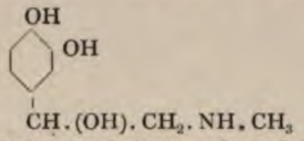


FIG. 316.—Section through a portion of the medullary part of the supra-renal of guinea-pig. The vessels are very numerous, and the fibrous stroma more distinct than in the cortex, and is, moreover, reticulated. The cells are irregular and larger, clear, and free from oil globules. (S. K. Alcock.)

muscles is to increase their tone, so that a tracing obtained from them resembles that produced by a small dose of veratrine, namely, a prolongation of the period of relaxation. The effect on involuntary muscle is equally marked; there is an enormous rise of arterial blood-pressure due chiefly to a contraction of the arterioles. This is produced by the direct action of the extract on the muscular tissue of the arterioles, not an indirect one through the vaso-motor centre.* The active substance in the extract that produces the effect is known as *adrenaline;* it is the reducing substance alluded to above which is confined to the medulla of the capsules, and is absent in cases of Addison's disease.

The capsules, therefore, form something which is distributed to the muscles and is essential for their normal tone; when they are removed or diseased the poisonous effects seen are the result of the absence of this internal secretion.

Adrenaline has received various names from the different chemists (Abel, v. Fürth, Takamine, etc.), who have isolated it. It is very powerful; solutions of one part in a million will produce physiological effects. Its composition is shown by the following formula:—



$$C_6H_3(OH)_2 \cdot CH.(OH).CH_2.NH.CH_3$$

and it is therefore a methyl-amino derivation of catechol (Pauly, Jowett). Recently compounds closely allied to it have been made synthetically (Stolz, Friedmann, Dakin).

Whether this discovery will lead to the same kind of results, as in the case of the thyroid, must be left to the future to decide. There is already some evidence to show that injection of supra-renal extract is beneficial in cases of Addison's disease. The discovery of adrenaline itself is, however, one of immense practical importance. Its action on the small blood-vessels is so powerful that quite weak solutions applied locally will arrest hæmorrhage.

There are some points of interest in the development and comparative physiology of the supra-renals. In mammals the medullary portion is developed in connection with the sympathetic, and is at first distinct and outside the cortical portion which is developed in connection with the upper part of the Wolffian body; it gradually insinuates itself within the cortex (Mitsukiri). In Elasmobranch fishes the supra-renals consist throughout life of separate portions; one, the inter-renal body, is median in position and single; this corresponds to the cortex of the mammalian supra-renal; extracts of this are inactive, and in the Teleostean fishes, where it is the sole representative of the supra-renal, it may be removed without any harm to the animal. The other portion of the Elasmobranch supra-renal is paired, and derived from the sympathetic ganglia. This corresponds to the medulla; it contains the same chromogen as the medulla of the mammalian supra-renal, and extracts of it have the same physiological action (S. Vincent).

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* Although muscular tissue is spoken of in the above description, Brodie's work shows that it is the sympathetic nerve terminals which are really affected.

The Pituitary Body.

This body is a small reddish-grey mass, occupying the sella turcica of the sphenoid bone. It consists of two lobes—a small posterior one, and an anterior larger one, somewhat resembling the thyroid in structure. The anterior lobe is developed as a tubular prolongation from the epiblast of the buccal cavity. The growth of intervening tissue soon cuts off all connection with the mouth. The alveoli are approximately spherical; they are filled with nucleated cells of various sizes and shapes not unlike ganglion cells, collected together into rounded masses, filling the vesicles, and contained in a colloid substance. The vesicles are enclosed by connective-tissue, rich in capillaries. The posterior lobe is developed from the floor of the third ventricle; it consists mainly of vascular connective tissue, and includes masses of epithelial cells. In the adult it contains no distinct nerve-cells, but it receives nerve-fibres which originate in the grey matter behind the optic chiasma.

Disease of the pituitary body produces the condition called *acromegaly*, in which the bones of limbs and face hypertrophy. When the gland is removed in animals, tremors and spasms occur like those which take place after removal of the thyroid. Death usually occurs within fourteen days. Some observers have stated that overgrowth of the pituitary occurs after excision of the thyroid. But there is no ground for the assumption that the two glands have a similar function. Acromegaly is a very different disease from myxœdema. The injection of extracts of the organs are also different. Thyroid extract produces a fall of arterial pressure. Extracts of the anterior lobe of the pituitary body are inactive; but extracts of the posterior lobe or infundibular body contain two active substances, one of which produces a rise, and the other a fall of blood-pressure. A second dose of the former of these injected soon after the first dose is inactive; and so it is not the same thing as in supra-renal extract. The chemical nature of the two substances is not known. Pituitary extracts when injected into the blood also produce diuresis (Schäfer).

The Pineal Gland.

This gland, which is a small reddish body, is placed beneath the back part of the corpus callosum, and rests upon the corpora quadrigemina. It is composed of tubes and saccules lined and sometimes filled with epithelial cells, and containing deposits of earthy salts (brain sand). These are separated by vascular connective tissue. A few small atrophied nerve-cells without axons are also seen.

In certain lizards, such as Hatteria, the pineal gland is better developed and is connected by nerve-fibres to a rudimentary third eye situated centrally on the upper surface of the head, but covered by skin.

The Coccygeal and Carotid Glands.

These so-called glands are situated, the one in front of the tip of the coccyx and the other at the point of bifurcation of the common carotid artery on each side. They are made up of a plexus of small arteries, and are enclosed and supported by a capsule of fibrous tissue. They contain also polyhedral cells collected into spheroidal clumps (carotid gland) or irregular nodules (coccygeal gland). Some of the cells of the carotid gland stain brown with chromic acid like those of the supra-renal medulla.

CHAPTER XXIV

RESPIRATION

THE respiratory apparatus consists of the lungs and of the air-passages which lead to them. In marine animals the gills fulfil the same functions as the lungs of air-breathing animals. The muscles which move the thorax and the nerves that supply them must also be included under the general heading Respiratory System; and, using this expression in the widest sense, it includes practically all the tissues of the body, since they are all concerned in the using up of oxygen and the production of waste materials, like carbonic acid.

Essentially a lung or gill is constructed of a thin membrane, one surface of which is exposed to the air or water, as the case may be, while, on the other is a network of blood-vessels—the only separation between the blood and aërating medium being the thin wall of the blood-vessels, and the fine membrane on one side of which vessels are distributed. The difference between the simplest and the most complicated respiratory membrane is one of degree only.

The lungs or gills are only the medium for the *exchange*, on the part of the blood, of carbonic acid for oxygen. They are not the seat, in any special manner, of those combustion-processes of which the production of carbonic acid is the final result. These processes occur in all parts of the body in the substance of the tissues.

The Respiratory Apparatus.

The lungs are contained in the chest or thorax, which is a closed cavity having no communication with the outside except by means of the respiratory passages. The air enters these passages through the nostrils or through the mouth, whence it passes through the larynx into the trachea or windpipe, which about the middle of the chest divides into two tubes, bronchi, one to each (right and left) lung.

The *Larynx* is the upper part of the passage, and will be described in connection with the voice.

The Trachea and Bronchi.—The trachea extends from the cricoid cartilage, which is on a level with the fifth cervical vertebra, to a point opposite the third dorsal vertebra, where it divides into the two bronchi, one for each lung (fig. 317). It measures, on an average, four or four and a half inches in length and from three-quarters of an inch to an inch in diameter, and is essentially a tube of fibro-elastic membrane, within the layers of which are imbedded a series of cartilaginous rings, from sixteen to twenty in number. These rings ex-

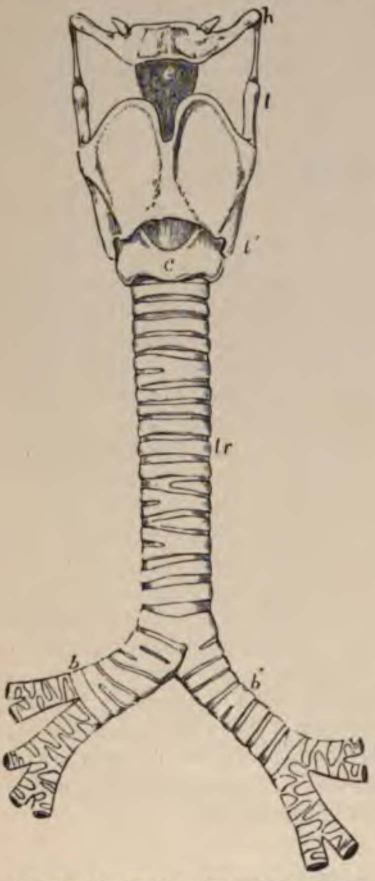

FIG. 317.—Outline showing the general form of the larynx, trachea, and bronchi, as seen from the front. *h*, The great cornu of the hyoid bone: *e*, epiglottis; *t*, superior, and *t'*, inferior cornu of the thyroid cartilage; *c*, middle of the cricoid cartilage; *tr*, the trachea, showing sixteen cartilaginous rings; *b*, the right, and *b'*, the left bronchus. (Allen Thomson.)

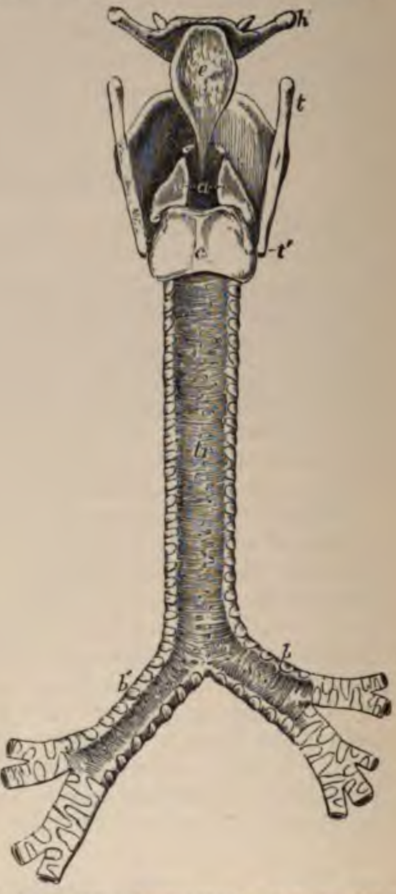

FIG. 318.—Outline showing the general form of the larynx, trachea, and bronchi, as seen from behind. *h*, Great cornu of the hyoid bone; *t*, superior, and *t'*, the inferior cornu of the thyroid cartilage; *e*, epiglottis; *a*, points to the back of both the arytenoid cartilages, which are surmounted by the cornicula; *c*, the middle ridge on the back of the cricoid cartilage; *tr*, the posterior membranous part of the trachea; *b*, *b'*, right and left bronchi. (Allen Thomson.)

tend only around the front and sides of the trachea (about two-thirds of its circumference) and are deficient behind; the interval between their posterior extremities is bridged over by a continuation of the fibrous membrane in which they are enclosed (fig. 318). The cartilages of the trachea and bronchial tubes are of the hyaline variety.

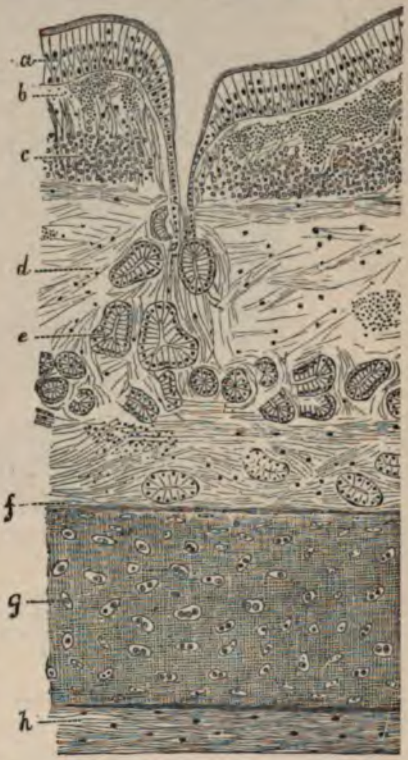

FIG. 319.—Section of the trachea. *a*, columnar ciliated epithelium; *b* and *c*, corium of the mucous membrane, containing elastic fibres cut across transversely; *d*, submucous tissue containing mucous glands, *e*, separated from the hyaline cartilage, *g*, by fine fibrous tissue, *f*; *h*, external investment of fine fibrous tissue. (S. K. Alcock.)

Immediately within this tube, at the back, is a layer of unstriped muscular fibres, which extends, *transversely*, between the ends of the cartilaginous rings to which they are attached, and opposite the intervals between them also; their function is to diminish, when required, the calibre of the trachea by approximating the ends of the cartilages. Outside these are a few *longitudinal* bundles of muscular tissue, which, like the preceding, are attached both to the fibrous and cartilaginous framework.

The mucous membrane consists to a great extent of loose lymphoid tissue, separated from the ciliated epithelium (fig. 322) which lines it by a homogeneous basement membrane. In the deeper part of the corium of the mucous membrane are many elastic fibres, between which lie connective-tissue corpuscles and capillary blood-vessels.

Numerous mucous glands are situated in the substance of the mucous membrane of the trachea; their ducts perforate the various structures which form the wall of the trachea, and open through the mucous membrane into the interior (fig. 319).

The two bronchi into which the trachea divides, of which the right is shorter, broader, and more horizontal than the left (fig. 317), resemble the trachea in structure, with the difference that in them there is a distinct layer of unstriped muscle arranged circularly beneath the mucous membrane, forming the *muscularis mucosæ*. On entering the substance of the lungs the cartilaginous rings, although they still form only larger or smaller segments of a circle, are no longer confined to the front and sides of the tubes, but are distributed impartially to all parts of their circumference.

The bronchi divide and subdivide, in the substance of the lungs, into a number of smaller and smaller branches (bronchial tubes), which penetrate into every part of the organ, until at length they end in the smaller subdivisions of the lungs called *lobules.*

All the larger branches have walls formed of fibrous tissue, containing portions of cartilaginous rings, by which they are held open, and unstriped muscular fibres, as well as longitudinal bundles of elastic tissue. They are lined by mucous membrane the surface of which, like that of the larynx and trachea, is covered with ciliated epithelium, but the several layers become less and less distinct until the lining consists of a single layer of short columnar cells covered with cilia (fig. 320). The mucous membrane is abundantly provided with mucous glands.

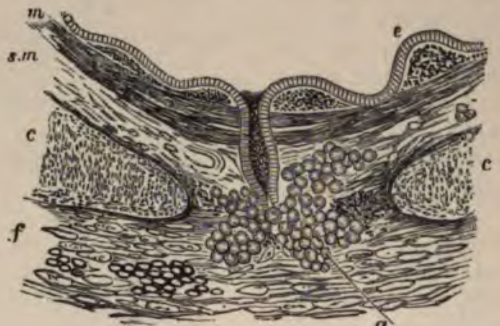

FIG. 320.—Transverse section of a bronchial tube, about $\frac{1}{4}$ inch in diameter. *e*, Epithelium (ciliated); immediately beneath it is the corium of the mucous membrane, of varying thickness; *m*, muscular layer; *s.m*, submucous tissue; *f*, fibrous tissue; *c*, cartilage enclosed within the layers of fibrous tissue; *g*, mucous gland. (F. E. Schulze.)

As the subdivisions become smaller and smaller, and their walls thinner, the cartilaginous rings become scarcer and more irregular, until, in the smaller bronchial tubes, they are represented only by minute and scattered cartilaginous flakes. When the bronchial tubes, by successive branchings, are reduced to about $\frac{1}{40}$ of an inch (·6 mm.) in diameter they lose their cartilaginous element altogether, and their walls are formed only of a fibrous elastic membrane with circular muscular fibres; they are still lined, however, by a thin mucous membrane with ciliated epithelium, the length of the cells bearing the cilia having become so far diminished that the cells are now cubical. In the smaller bronchial tubes the muscular fibres are relatively more abundant than in the larger ones, and form a distinct circular coat.

The Lungs and Pleuræ.—The lungs occupy the greater portion of the thorax. They are of a spongy elastic texture, and are composed of numerous minute air-sacs, and on section every here and there the air-tubes may be seen cut across. Any fragment of lung (unless from a child that has never breathed, or in cases of disease in which the lung is consolidated) floats in water; no other tissue does this.

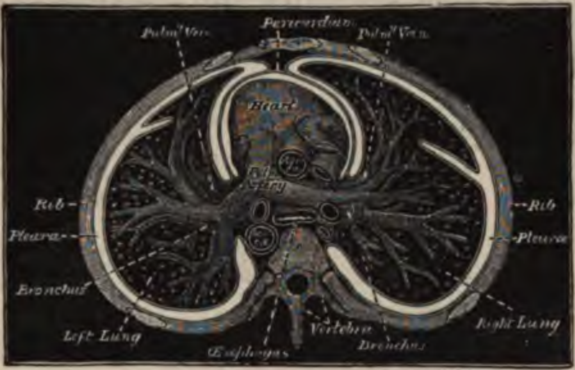

FIG. 321.—Transverse section of the chest.

Each lung is enveloped by a serous membrane—the *pleura*, one layer of which adheres closely to its surface, and provides it with its smooth and slippery covering, while the other adheres to the inner surface of the chest-wall. The continuity of the two layers, which form a closed sac, as in the case of other serous membranes, will be best understood by reference to fig. 321. The appearance of a space, however, between the pleura which covers the lung (*visceral* layer) and that which lines the inner surface of the chest (*parietal* layer) is inserted in the drawing only for the sake of distinctness. It does not really exist. The layers are, in health, everywhere in contact one with the other; and between them is only just so much fluid as will ensure the lungs gliding easily, in their expansion and contraction, on the inner surface of the parietal layer, which lines the chest-wall.

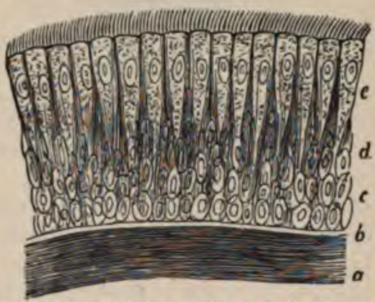

FIG. 322.—Ciliated epithelium of the human trachea. *a*, Layer of longitudinally arranged elastic fibres; *b*, basement membrane; *c*, deepest cells circular in form; *d*, intermediate elongated cells; *e*, outermost layer of cells fully developed and bearing cilia. × 350. (Kölliker.)

If, however, an opening is made so as to permit air or fluid to enter the pleural sac, the lung, in virtue of its elasticity, recoils, and a considerable space is left between it and the chest-wall. In other words, the natural elasticity of the lungs would cause them at all times to contract away from the ribs were it not that the contraction is resisted by atmospheric pressure which bears only on the *inner* surface of the air-tubes and air-sacs. On the admission of air into the pleural sac atmospheric pressure bears alike on the inner and outer surfaces of the lung, and their elastic recoil is no longer prevented.

Each lung is partially subdivided into separate portions called *lobes;* the right lung into three lobes, and the left into two. Each of these lobes, again, is composed of a large number of minute parts, called *lobules.* Each pulmonary lobule may be considered to be a lung in miniature, consisting, as it does, of a branch of the bronchial tube, of air-sacs, blood-vessels, nerves, and lymphatics, with a sparing amount of areolar tissue.

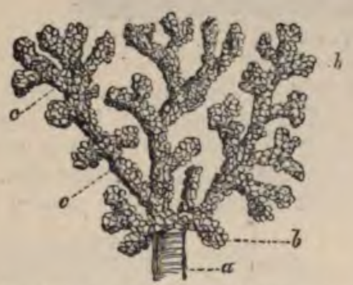

FIG. 323.—Terminal branch of a bronchial tube, with its infundibula and air-sacs, from the margin of the lung of a monkey, injected with quicksilver. *a*, Terminal bronchial twig; *b b*, infundibula and air-sacs. × 10. (F. E. Schulze.)

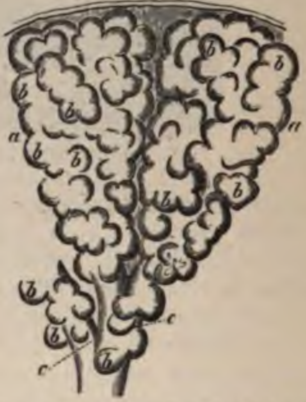

FIG. 324.—Two small infundibula or groups of air-sacs, *a a*, with air-sacs, *b b*, and the ultimate bronchial tubes, *c c*, with which the air-sacs communicate. From a new-born child. (Kölliker.)

On entering a lobule, the small bronchial tube, the structure of which has just been described (*a*, fig. 323), divides and subdivides; its walls at the same time become thinner and thinner, until at length they are formed only of a thin membrane of areolar, muscular, and elastic tissue, lined by a layer of pavement epithelium not provided with cilia. At the same time they are altered in shape; each of the minute terminal branches widens out funnel-wise, and its walls are pouched out irregularly into small saccular dilatations, called *air-sacs* (fig. 323, *b*). Such a funnel-shaped terminal branch of the bronchial tube, with its group of pouches or air-sacs, is called an *infundibulum* (figs. 323, 324), and the irregular oblong space in its centre, with which the air-sacs communicate, an *intercellular passage.*

The air-sacs, or air-vesicles, may be placed singly, like recesses from the intercellular passage, but more often they are arranged in groups, or even in rows, like minute sacculated tubes; so that a short series of vesicles, all communicating with one another, open by a common orifice into the tube. The vesicles are of various forms, according to the mutual pressure to which they are subject; their walls are nearly in contact, and they vary from $\frac{1}{50}$th to $\frac{1}{70}$th of an inch (·5 to ·3 mm.) in diameter. Their walls are formed of fine membrane, like those of the intercellular passage; this membrane is folded on itself so as to form a sharp-edged border at each circular orifice of communication between contiguous air-vesicles, or between the vesicles and the bronchial passages. Numerous fibres of elastic tissue are spread out between contiguous air-sacs, and many of these are attached to the outer surface of the fine membrane of which each sac is composed, imparting to it additional strength and the power of recoil after distension. The vesicles are lined by a layer of pavement epithelium (fig. 325) not provided with cilia. Outside the air-vesicles a network of pulmonary capillaries is spread out so densely (fig. 326) that the interspaces or meshes are even narrower than the vessels,

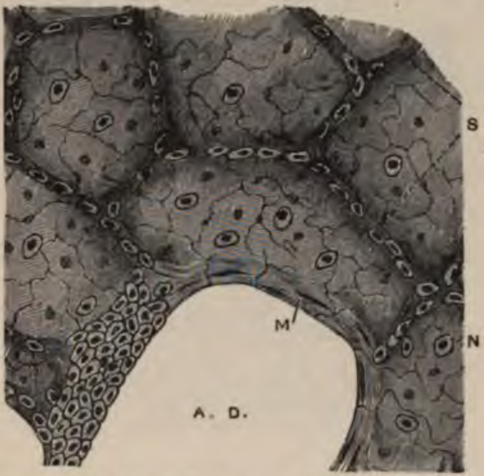

FIG. 325.—Section of lung stained with silver nitrate. A. D., alveolar duct or intercellular passage; S, alveolar septa; N, alveoli or air-sacs, lined with large flat cells, with some smaller polyhedral cells; M, plain muscular fibres surrounding the alveolar duct. (Klein and Noble Smith.)

which are, on an average, $\frac{1}{3000}$th of an inch (8μ) in diameter. Between the air in the sacs and the blood in these vessels nothing intervenes but the thin walls of the air-sacs and of the capillaries; and the exposure of the blood to the air is the more complete, because the folds of membrane between contiguous air-sacs, and often the spaces between the walls of the same, contain only a single layer of capillaries, both sides of which are thus at once exposed to the air. The arrangement of the capillaries is shown on a larger scale in fig. 233 (p. 222).

The vesicles of adjacent lobules do not communicate; so that, when any bronchial tube is closed or obstructed, the supply of air is lost for all the sacs opening into it or its branches.

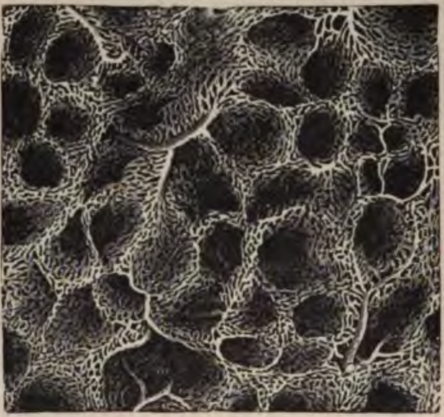

FIG. 326.—Capillary network of the pulmonary blood-vessels in the human lung. × 60. (Kölliker.)

Blood-supply.—The lungs receive blood from two sources, (*a*) the pulmonary artery, (*b*) the bronchial arteries. The former conveys *venous* blood to the lungs to be *arterialised*, and this blood takes no share in the nutrition of the pulmonary tissues through which it passes. The branches of the bronchial arteries convey arterial blood from the aorta for the nutrition of the walls of the bronchi, of the larger pulmonary vessels, of the interlobular connective-tissue, etc.; the blood of the bronchial vessels is returned chiefly through the bronchial and partly through the pulmonary veins.

Lymphatics.—The lymphatics are arranged in three sets:—1. Irregular lacunæ in the walls of the alveoli or air-sacs. The lymphatic vessels which lead from these accompany the pulmonary vessels towards the root of the lung. 2. Irregular anastomosing spaces in the walls of the bronchi. 3. Lymph-spaces in the pulmonary pleura. The lymphatic vessels from all these irregular sinuses pass in towards the root of the lung to reach the bronchial lymphatic glands.

Nerves.—The nerves of the lung are to be traced from the anterior and posterior pulmonary plexuses, which are formed by branches of the vagus and sympathetic. The nerves follow the course of the vessels and bronchi, and in the walls of the latter many small ganglia are situated.

The Respiratory Mechanism.

Respiration consists of the alternate expansion and contraction of the thorax, by means of which air is drawn into or expelled from the lungs. These acts are called *Inspiration* and *Expiration* respectively.

For the inspiration of air into the lungs it is evident that all that is necessary is such a movement of the side-walls or floor of the chest, or of both, that the capacity of the interior shall be enlarged. By such increase of capacity there will be a diminution of the pressure of the air in the lungs, and a fresh quantity will enter through the larynx and trachea to equalise the pressure on the inside and outside of the chest.

For the expiration of air, on the other hand, it is also evident that, by an opposite movement which shall diminish the capacity of the chest, the pressure in the interior will be increased, and air will be expelled, until the pressure within and without the chest are again equal. In both cases the air passes through the trachea and larynx, whether in entering or leaving the lungs, there being no other communication with the exterior of the body; and the lung, for the same reason, remains, under all the circumstances described, closely in contact with the walls and floor of the chest. To speak of expansion of the chest, is to speak also of expansion of the lung. The movements of the lung are therefore passive, not active, and depend on the changes of shape of the closed cavity in which they are contained. A perforation of the chest-wall would mean that the lung on that side would no longer be of use; a similar injury on the other side (double pneumothorax) would cause death. If the two layers of the pleura were adherent, those portions of the lung would be expanded most where the movements of the chest are greatest. The existence of the two layers prevents this, and thus the lung is equally expanded throughout.

Inspiration.—The enlargement of the chest in inspiration is a muscular act; the effect of the action of the inspiratory muscles is an increase in the size of the chest-cavity in the vertical, and in the lateral and antero-posterior diameters. The muscles engaged in *ordinary* inspiration are the diaphragm; the external intercostals; parts of the internal intercostals; the levatores costarum; and serratus posticus superior.

The *vertical diameter* of the chest is increased by the contraction and consequent descent of the diaphragm; at rest, the diaphragm is dome-shaped with the convexity upwards; the central tendon forms a slight depression in the middle of this dome. On contraction the muscular fibres shorten, and so the convexity of the double dome is lessened. The central tendon, which was formerly regarded as remaining fixed, is drawn down a certain distance, but the chief movement is at the sides. For the effective action of this muscle, its attachment to the lower ribs is kept fixed by the contraction of the quadratus lumborum. The diaphragm is supplied by the *phrenic* nerves.

The increase in the *lateral* and *antero-posterior diameters* of the chest is effected by the raising of the ribs, the upper ones being fixed by the scaleni. The greater number of the ribs are attached very obliquely to the spine and sternum.

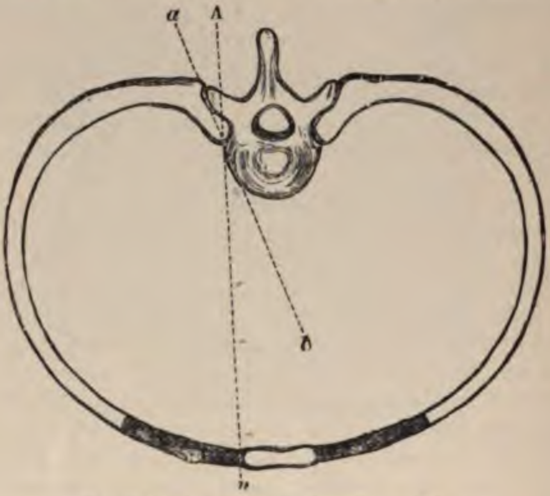

FIG. 327.—Diagram of axes of movement of ribs.

The elevation of the ribs takes place both in front and at the sides—the hinder ends being prevented from performing any upward movement by their attachment to the spine. The movement of the front extremities of the ribs is of necessity accompanied by an upward and forward movement of the sternum to which they are attached, the movement being greater at the lower end than at the upper end of the latter bone.

The axes of rotation in these movements are two: one corresponding with a line drawn through the two articulations which the rib forms with the spine (*a*, *b*, fig. 327); and the other with a line drawn from one of these (head of rib) to the sternum (A B, fig. 327); the motion of the rib around the latter axis being somewhat after the fashion of raising the handle of a bucket.

The elevation of the ribs is accompanied by a slight opening out of the angle which the bony part forms with its cartilage; and thus an additional means is provided for increasing the antero-posterior diameter of the chest.

The muscles by which the ribs are raised, in *ordinary* quiet inspiration, are the *external intercostals*, and that portion of the *internal intercostals* which is situated between the costal cartilages; and these are assisted by the *levatores costarum*, and the *serratus posticus superior*.

In tranquil breathing, the expansive movements of the lower part of the chest are greater than those of the upper. In forced inspiration, on the other hand, the greatest extent of movement appears to be in the upper antero-posterior diameter.

In *extraordinary* or forced inspiration, as in violent exercise, or in cases in which there is some interference with the due entrance of air into the chest, and in which, therefore, strong efforts are necessary, other muscles than those just enumerated are pressed into service. It is impossible to separate by a hard-and-fast line the muscles of *ordinary* from those of *extraordinary* inspiration; but there is no doubt that the following are but little used as *respiratory* agents, except in cases in which unusual efforts are required—the *sterno-mastoid*, the *serratus magnus*, the *pectorales*, and the *trapezius*. Laryngeal and face muscles also come into play.

The expansion of the chest in inspiration presents some peculiarities in different persons. In young children, it is effected chiefly by the diaphragm, which being highly arched in expiration, becomes flatter as it contracts, and, descending, presses on the abdominal viscera, and pushes forward the front walls of the abdomen. The movement of the abdominal walls being here more manifest than that of any other part, it is usual to call this the *abdominal* type of respiration. In men, together with the descent of the diaphragm, and the pushing forward of the front wall of the abdomen, the chest and the sternum are subject to a wide movement in inspiration (*inferior costal* type). In women, the movement appears less extensive in the lower, and more so in the upper, part of the chest (*superior costal* type).

There are also differences in different animals. In the frog, for example, the air is forced into the lungs by the raising of the floor of the mouth, the mouth and nostrils being closed.

Expiration.—From the enlargement produced in inspiration, the chest and lungs return, in ordinary tranquil expiration, by their elasticity; the force employed by the inspiratory muscles in distending the chest and overcoming the elastic resistance of the lungs and chest-walls, is returned as an expiratory effort when the muscles are relaxed. This elastic recoil of the chest and lungs is sufficient, in ordinary quiet breathing, to expel air from the lungs in the intervals of inspiration, and no muscular power is required. In all voluntary expiratory efforts, however, as in speaking, singing, blowing, and the like, and in many involuntary actions also, as sneezing, coughing, etc., something more than merely passive elastic power is necessary, and the proper expiratory muscles are brought into action. By far the chief of these are the abdominal muscles, which, by pressing on the viscera of the abdomen, push up the floor of the chest formed by the diaphragm, and by thus making pressure on the lungs, expel air from them through the trachea and larynx. All muscles, however, which depress the ribs, must act also as muscles of expiration, and therefore we must conclude that the abdominal muscles are assisted in their action by the interosseous part of the *internal intercostals*, the *triangularis sterni*, the *serratus posticus inferior*, and *quadratus lumborum*. When by the efforts of the expiratory muscles, the chest has been squeezed to less than its average diameter, it again, on relaxation of the muscles, returns to the normal dimensions by virtue of its elasticity. The construction of the chest-walls, therefore, admirably adapts them for recoiling against and resisting as well undue contraction as undue dilatation. In the natural condition of the parts, the lungs can never contract to the utmost, but are always more or less "on the stretch," being kept closely in contact with the inner surface of the chest walls.

Methods of recording Respiratory Movements.

The movements of respiration may be recorded graphically in several ways. One method is to introduce a tube into the trachea of an animal, and to connect this tube by some gutta-percha tubing with a T-piece introduced into the cork of a large bottle, the other end of the T having attached to it a second piece of tubing, which can remain open or can be partially or completely closed by means of a screw clamp. Into the cork is inserted a second piece of glass tubing connected with a Marey's tambour by suitable tubing. This second tube communicates any alteration of the pressure in the bottle to the tambour, and this may be made to write on a recording surface.

There are various instruments for recording the movements of the chest by application of apparatus to the exterior. Such is the **stethograph** of Burdon-Sanderson (fig. 329). This consists of a frame formed of two parallel steel bars joined by a third at one end. At the free end of the bars is attached a leather strap, by means of which the apparatus may be suspended from the neck. Attached to the inner end of one bar is a tambour and ivory button, to the end of the other an ivory button. When in use, the apparatus is suspended with the transverse bar posteriorly, the button of the tambour is placed on the part of the chest the movement of which it is desired to record, and the other button is made to press upon the corresponding point on the other side of the chest, so that the chest is, as it were, held between a pair of callipers. The tambour is connected by tubing and a T-piece with a recording tambour and with a ball, by means of which air can be squeezed into the cavity of the tambour. When in work the tube connected with the air ball is shut off by means of a screw clamp. The movement of the chest is thus communicated to the recording tambour.

A simpler form of this apparatus consists of a thick india-rubber bag of elliptical shape about three inches long, to one end of which a rigid gutta-percha tube is attached. This bag may be fixed at any required place on the chest by means of a strap and buckle. By means of the gutta-percha tube the variations of the pres-

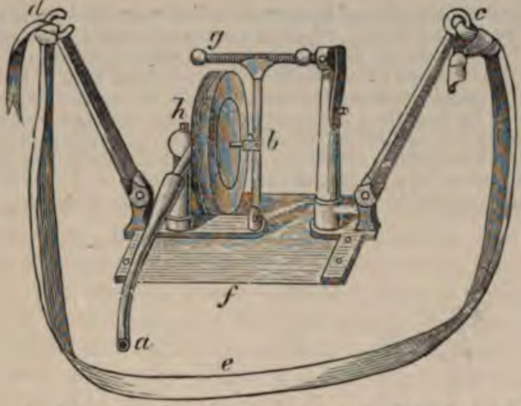

FIG. 328.—Stethograph. *h*, tambour fixed at right angles to plate of steel *f*; *c* and *d*, arms by which instrument is attached to chest by belt *e*. When the chest expands, the arms are pulled asunder, which bends the steel plate, and the tambour is affected by the pressure of *b*, which is attached to it on the one hand, and to the upright in connection with horizontal screw *g*. (Modified from Marey's instrument.)

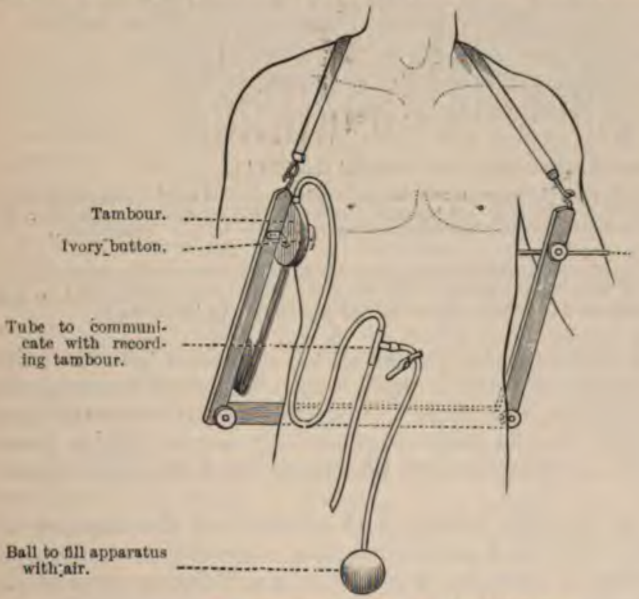
Tambour.
Ivory button.
Tube to communicate with recording tambour.
Ball to fill apparatus with air.

FIG. 329.—Stethograph. (Burdon-Sanderson.)

sure of air in the bag produced by the movements of the chest are communicated to a recording tambour. This apparatus is a simplified form of Marey's stethograph (fig. 328).

The variations of intrapleural pressure may be recorded by the introduction of a cannula into the pleural cavity, which is connected with a mercurial manometer.

Finally, it has been found possible in various ways to record the diaphragmatic movements by the insertion of an elastic bag connected with a tambour into the abdomen below it (**phrenograph**), by the insertion of needles into different parts of its structure, or by recording the contraction of isolated strips of the diaphragm. Such a strip attached in the rabbit to the xiphisternal cartilage may be detached, and attached by a thread to a recording lever. This method was largely used by Head; this strip serves as a sample of the diaphragm.

Fig. 330 shows a tracing obtained in this way; but in tracings taken with a stethograph, or any of the numerous arrangements of tambours which are applied to the chest-walls of men and animals, the large up-and-down strokes due to the respiratory movements have upon them smaller waves due to heart-beats.

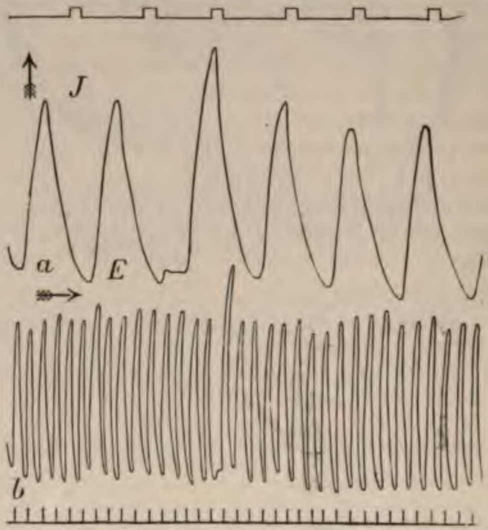

FIG. 330.—Tracing of the normal diaphragm respirations of rabbit. *a*, with quick movement of drum. *b*, with slow movement. The upstrokes represent inspiration; the downstrokes, expiration. To be read from left to right. The time tracing in each case represents seconds. (Marckwald.)

The acts of expansion and contraction of the chest take up under ordinary circumstances a nearly equal time. The act of inspiring air, however, especially in women and children, is a little shorter than that of expelling it, and there is commonly a very slight pause between the end of expiration and the beginning of the next inspiration.

If the ear be placed in contact with the wall of the chest, or be separated from it only by a good conductor of sound or stethoscope, a faint *respiratory* or *vesicular murmur* is heard during inspiration. This sound varies somewhat in different parts—being loudest or coarsest in the neighbourhood of the trachea and large bronchi (tracheal and bronchial breathing), and fading off into a faint sighing as the ear is placed at a distance from these (vesicular breathing). It is best heard in children, and in them a faint murmur is heard in expiration also. The cause of the vesicular murmur has received various explanations; but most observers hold that the sound is produced by the air passing through the glottis and larger tubes, and that this sound is modified in its conduction through the substance of the lung. The alterations in the normal breath sounds, and the various additions to them that occur in different diseased conditions, can only be properly studied at the bedside.

Respiratory movements of the Nostrils and of the Glottis.—During the action of the muscles which directly draw air into the chest, those which guard the opening through which it enters are not passive. In hurried breathing the instinctive dilatation of the nostrils is well seen, although under ordinary conditions it may not be noticeable. The opening at the upper part of the larynx or rima glottidis is slightly dilated at each inspiration for the more ready passage of air, and becomes smaller at each expiration; its condition, therefore, corresponds during respiration with that of the walls of the chest. There is a further likeness between the two acts in that, under ordinary circumstances, the dilatation of the rima glottidis is a muscular act and its narrowing chiefly an elastic recoil.

Terms used to express Quantity of Air breathed.—a. *Tidal air* is the quantity of air which is habitually and almost uniformly changed in each act of breathing. In a healthy adult man it is about 20 cubic inches, or about 300 c.c. It will be seen that this amount of air is not nearly sufficient to fill the lungs; it fills the upper respiratory passages; Zuntz gives the capacity of the upper air passages and bronchial tubes as 140 c.c., and if this low estimate is correct, about half the tidal air is required to fill this space. At the end of an expiration, however, the tubes and alveoli are not empty of air, and the sudden inrush of atmospheric air during inspiration effects a complete mixture of this air with that left in the air passages; it is possible that the air in the axial stream of the current may penetrate as far even as the alveoli, but what is sucked into the alveoli is mainly some of the mixture from the bronchial passages, and that in turn is derived from the mixture (containing more atmospheric air in proportion) in the upper air cavities. During expiration the air which leaves the lungs may come in part from the alveoli, but the effect of the stream of outgoing air is mainly as before to effect a thorough admixture of the air in the intermediate air passages; thus the alveolar air will become mixed with that in the bronchial tubes, and that in turn will be mixed with that in the upper air chambers. In a succession of alternate inspirations and expirations adequate ventilation is secured, but obviously the composition of the expired air is not the same as that of alveolar air, for the latter, though it is ultimately breathed out, is diluted on its upward journey by mixture with the bronchial air, and that in its turn with the air of the upper air chambers; in other words, the expired air is alveolar air (rich in carbon dioxide) diluted with bronchial air (richer in oxygen) and with atmospheric air (still richer in oxygen). No doubt diffusion of gases occurs as well, oxygen diffusing inwards and carbon dioxide outwards, but this molecular movement is too slow to be of any real use in aërating the blood, for almost immediately the respiratory movements cease, death occurs.

b. *Complemental air* is the quantity over and above this which can be drawn into the lungs in the deepest inspiration; its amount varies, but it may be reckoned as 100 cubic inches, or about 1600 c.c.

c. *Reserve* or *supplemental air.*—After ordinary expiration, such as that which expels the breathing or tidal air, a certain quantity of air, about 100 cubic inches (1600 c.c.) remains in the lungs, which may be expelled by a forcible and deeper expiration. This is termed *reserve* or *supplemental air.*

d. *Residual air* is the quantity which still remains in the lungs after the most violent expiratory effort. Its amount depends in great measure on the absolute size of the chest, but may be estimated at about 100 cubic inches, or about 1600 c.c.

The total quantity of air which passes into and out of the lungs of an adult, at rest, in 24 hours, varies from 400,000 (Marcet) to 680,000 (Hutchinson) cubic inches. This quantity, however, is increased, and may be more than doubled by exertion.

e. *Respiratory* or *Vital Capacity.*—The vital capacity of the chest is indicated by the quantity of air which a person can expel from his lungs by a forcible expiration after the deepest inspiration possible. The average capacity of an adult, at 15·4° C. (60° F.), is about 225 to 250 cubic inches, or 3500 to 4000 c.c. It is the sum of the complemental, tidal, and supplemental air.

The *respiratory* capacity, or as John Hutchinson called it, *vital* capacity, is usually measured by a modified gasometer or *spirometer*, into which the experimenter breathes,—making the most prolonged expiration possible after the deepest possible inspiration. The quantity of air which is thus expelled from the lungs is indicated by the height to which the air-chamber of the spirometer rises; and by means of a scale placed in connection with this, the number of cubic inches is read off.

In healthy men, the respiratory capacity varies chiefly with the stature, weight, and age.

It was found by Hutchinson, from whom most of our information on this subject is derived, that at a temperature of 15·4° C. (60° F.), 225 cubic inches is the average *vital* or respiratory capacity of a healthy person, five feet seven inches in height.

Circumstances affecting the amount of respiratory capacity.—For every inch of height above this standard the capacity is increased, on an average, by eight cubic inches; and for every inch below, it is diminished by the same amount.

The influence of *weight* on the capacity of respiration is less manifest and considerable than that of height; and it is difficult to arrive at any definite conclusions on this point, because the natural average weight of a healthy man in relation to stature has not yet been determined. As a general statement, however, it may be said that the capacity of respiration is not affected by weights under 161 pounds, or 11½ stones; but that, above this point, it is diminished at the rate of one cubic inch for every additional pound up to 196 pounds, or 14 stones.

By *age*, the capacity is increased from about the fifteenth to the thirty-fifth year, at the rate of five cubic inches per year; from thirty-five to sixty-five it diminishes at the rate of about one and a half cubic inch per year; so that the capacity of respiration of a man of sixty years old would be about 30 cubic inches less than that of a man forty years old, of the same height and weight.

Sex.—The vital capacity of an adult man to that of a woman of the same height is 10 to 7.

The *number* of respirations in a healthy adult person usually ranges from 14 to 18 per minute. It is greater in infancy and childhood. It varies also much according to different circumstances, such as exercise or rest, health or disease, etc. Variations in the number of respirations correspond ordinarily with similar variations in the pulsations of the heart. In health the proportion is about 1 to 4, or 1 to 5, and when the rapidity of the heart's action is increased, that of the chest movement is commonly increased also; but not in every case in equal proportion. It happens occasionally in disease, especially of the lungs or air-passages, that the number of *respiratory* acts increases in quicker proportion than the beats of the *pulse;* and, in other affections, much more commonly, that the number of the pulse-beats is greater in proportion than that of the respirations.

The Force of Inspiratory and Expiratory Muscles.—The force with which the inspiratory muscles are capable of acting is greatest in individuals of the height of from five feet seven inches to five feet eight inches, and will elevate a column of nearly three inches (about 60 mm.) of mercury. Above this height the force decreases as the stature increases; so that the average of men of six feet can elevate only about two and a half inches of mercury. The force manifested in the strongest expiratory acts is, on the average, one-third greater than that exercised in inspiration. But this difference is in great measure due to the power exerted by the elastic reaction of the walls of the chest; and it is also much influenced by the disproportionate strength which the expiratory muscles attain, from their being called into use for other purposes than that of simple expiration. The force of the inspiratory act is, therefore, better adapted than that of the expiratory for testing the muscular strength of the body. (John Hutchinson.)

In ordinary quiet breathing, there is a negative pressure of only 1 mm. during inspiration, and a positive pressure of from 2 to 3 mm. mercury during expiration.

The instrument used by Hutchinson to gauge the inspiratory and expiratory power was a mercurial manometer, to which was attached a tube fitting the nostrils, and through which the inspiratory or expiratory effort was made.

The greater part of the force exerted in deep inspiration is employed in overcoming the resistance offered by the elasticity of the lungs.

In man the pressure exerted by the elasticity of the lungs alone is about 6 mm. of mercury. This is estimated by tying a manometer into the trachea of a dead subject, and observing the rise of mercury that occurs on puncture of the chest-walls. If the chest is distended beforehand so as to imitate a forcible inspiration, a much larger rise (30 mm.) of the mercury is obtained. In the body this elastic force is assisted by the contraction of the plain muscular fibres of the alveoli and bronchial tubes, the pressure of which probably does not exceed 1 or 2 mm. Hutchinson calculated that the total force to be overcome by the muscles in the act of inspiring 200 cubic inches of air is more than 450 lbs.

It is possible that the contractile power which the bronchial tubes and air-vesicles possess, by means of their *muscular fibres*, may assist in expiration; but it is more likely that the chief purpose of this muscular tissue is to regulate and adapt, in some measure, the quantity of air admitted to the lungs, and to each part of them, according to the supply of blood: the muscular tissue also contracts upon and gradually expels collections of mucus, which may have accumulated within the tubes, and which cannot be ejected by forced expiratory efforts, owing to collapse or other morbid conditions of the portion of lung connected with the obstructed tubes (Gairdner).

The Nervous Mechanism of Respiration.

In the central nervous system there is a specialised small district called the *respiratory centre.* This gives out impulses which travel down the spinal cord to the centres of the spinal nerves that innervate the muscles of respiration. It also receives various afferent fibres, the most important of which are contained in the trunk of the vagus. The vagus is chiefly an afferent nerve in relation to respiration. It, however, also is in a minor degree efferent, for it supplies the muscular tissue of the lungs and bronchial tubes, and exercises a trophic influence on the lung.

The respiratory centre was discovered by Flourens; it is situated at the tip of the calamus scriptorius, and almost exactly coincides in position with the centre of the vagus. The existence of subsidiary respiratory centres in the spinal cord has been mooted, but the balance of experimental evidence is against their existence. Flourens found that when the respiratory centre is destroyed, respiration at once ceases, and the animal dies. He therefore called it the "vital knot" (nœud vitale).

The centre is affected not only by the afferent impulses which reach it from the vagus, but also by those from the cerebrum; so that we have a limited amount of voluntary control over the respiratory movements.

The sensory nerves of the skin have also an effect. The action of the air on the body of a new-born child is no doubt the principal afferent cause of the first respirations. During fœtal life, the need of the embryo for oxygen is very small, and is amply met by the transference of oxygen from the maternal blood through the thin walls of the fœtal capillaries in the placenta. The application of cold water to the skin always causes a deep inspiration; this is another instance of the reflex effect which follows stimulation of the cutaneous nerves. Stimulation of the central end of the splanchnics causes expiration. Stimulation of the central end of the glosso-pharyngeal causes an inhibition of the respiratory movements for a short period; this accounts for the very necessary cessation of breathing during swallowing. Stimulation of the central end of the cut superior laryngeal nerve, or of its terminations in the mucous membrane of the larynx, as when a crumb is "swallowed the wrong way," produces inhibition of inspiratory and increase of expiratory efforts, culminating in coughing.

These nerves, however, are none of them in constant action as the vagi are, and the influence of the vagus is somewhat complicated. Still, respiration continues after the vagi are cut. The character of the respiration becomes altered, especially if both nerves are severed; it is slower and deeper. This is due to the cessation of the impulses that normally run up the vagi to the respiratory centre. The animal, however, lives a considerable time; a warm-blooded animal usually dies after about a week or ten days from *vagus pneumonia*, due to the removal of trophic influences from the lungs. Cold-blooded animals live longer; they exhibit fatty degeneration of the heart-muscle also.

The question has been much debated whether the activity of the respiratory centre is *automatic* or *reflex;* that is to say, whether the rhythmic discharges proceeding from it depend on local changes induced by the condition of its blood supply, or on the repeated stimulations it receives by afferent nerves.

There appears every reason to believe that the centre has the power of automatism, but this is never excited under normal circumstances. Normally, the respiratory process is a series of reflex actions.

The evidence in favour of the automatic activity of the centre is the following:—

(1.) If the spinal cord is cut just below the bulb, respiration ceases, except in the case of the facial and laryngeal muscles, which are supplied by nerves that originate above the point of injury. The alæ nasi work vigorously. Such respiration is not effective in drawing any air into the chest, and so the animal soon dies; but the forcible efforts of these muscles show that the respiratory centre is in a state of activity, sending out impulses to them. If the two vagus nerves are cut, these movements continue; this shows that afferent impulses from the vagus are not essential. As the blood gets more and more venous, the movements become more pronounced. The question has arisen whether this increased activity of the respiratory centre is due to increase of carbonic acid, or decrease of oxygen in the blood which it receives. The balance of evidence shows that the increase in the carbonic acid is the more important of the two.

(2.) In asphyxia, one always gets great increase of respiratory activity, called *dyspnœa;* this is produced by the stimulation of the centre by venous blood. It is not due (or not wholly due) to the action of the venous blood on the terminations of the vagi in the lungs, as the same phenomenon occurs when these nerves are cut; and, moreover, dyspnœa takes place if the venous blood is allowed to circulate through the brain alone, and not through the lungs at all. For instance, it ensues when localised venosity of the blood is produced in the brain by ligature of the carotid and vertebral arteries.

But, as before stated, the normal activity of the respiratory centre is not automatic, it is reflex, and the principal afferent channel is the vagus. The way in which it works has been made out of recent years by Marckwald, Hering, and Head. The following is a brief *résumé* of Head's results:—

His method of recording the movements was by means of that convenient slip of the diaphragm which is found in rabbits (see p. 356).

His method of dividing the vagus was by freezing it; he laid it across a copper wire, the end of which was placed in a freezing mixture. This method is free from the disadvantage which a cut with a knife or scissors possesses, namely, a stimulation at the moment of section. On dividing one vagus, respiration became slightly slower and deeper; on dividing the second nerve, this effect was much more marked.

On exciting the central end of the divided nerve, inspiratory efforts increased until at last the diaphragm came to a standstill in the inspiratory position. But if a weak stimulus was employed, the reverse was the case; the expiratory efforts increased, inspiration becoming weaker and weaker, until at last the diaphragm stopped in the position of expiration. This result always follows stimulation of the superior laryngeal nerve.

Most of these facts were known previously, but the interpretation of them, in the light of further experiments immediately to be described, is the following:—

That there are in the vagus two sets of fibres, one of which produces an increased activity of the inspiratory part of the respiratory centre, and the other an increased activity of the expiratory part of that centre. Stimulation of the first stops expiration and produces inspiration; stimulation of the second does the reverse.

The question now is, What is it that normally produces this alternate stimulation of the two sets of fibres? If we discover this we shall discover the prime moving cause in the alternation of the inspiratory and expiratory acts. It was sought and found in the alternate distension and contraction of the air-vesicles of the lungs where the vagus terminations are situated.

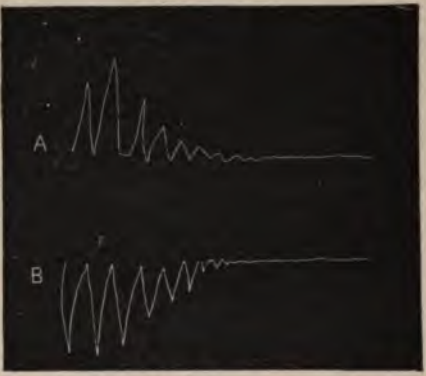

FIG. 331.—Tracings of diaphragm. The upward movements of the tracings represent inspiration; the downward movements, expiration. A, result of positive, B, of negative ventilation. (After Head.)

In one series of experiments *positive ventilation* was performed; that is, air was pumped repeatedly into the lungs, and so increased their normal distension; this was found to decrease the inspiratory contractions of the diaphragm, until at last they ceased altogether, and the diaphragm stood still in the expiratory position (fig. 331, A).

In a second series of experiments, *negative ventilation* was performed; that is, the air was pumped repeatedly out of the lungs, and a condition of collapse of the air-vesicles produced. This was found to increase the inspiratory contractions of the diaphragm, expiration became less and less, and at last the diaphragm assumed the position of inspiratory standstill (fig. 331, B).

Distension of the air-vesicles, therefore, stimulates the fibres of the vagus which excite the expiratory phase of respiration; collapse stimulates those which excite the inspiratory phase.

Ordinary respiration is an alternate positive and negative ventilation, though not so excessive as in the experiments just described. Inspiration is positive ventilation, and so provides the nervous mechanism of respiration with a stimulus that leads to expiration. Expiration is a negative ventilation, and so provides the stimulus that leads to inspiration.

It is probable that of the two sets of impulses, those which are started by the inspiratory movement play a more active part in the regulation of respiration than those started by the expiratory movement. Gad explains the latter by supposing they are simply due to a cessation of the former, or, in other words, that there only exists one class of afferent fibres in the vagus concerned in respiration. This view has not, however, met with general acceptance, and is against the mass of experimental evidence.

Apnœa.—If positive and negative ventilation are used together rapidly and alternately at a rate quicker than the respiratory rhythm, both inspiratory and expiratory processes are inhibited, and the respiration ceases for a short time. This follows naturally from the experiments previously described. This can be done on an animal with a pair of bellows fixed to a tube in the trachea; or voluntarily by oneself taking a number of deep breaths rapidly. This condition, called *apnœa*, is not due, as at one time supposed, to over-oxygenation of the blood, but is produced reflexly. Under normal circumstances arterial blood is always fully oxygenated. It is observed if inert gases, like nitrogen or hydrogen, are used instead of air. The pause, however, is then shorter, as the blood becomes venous, and in a short time stimulates the respiratory centre to activity.

Under abnormal circumstances, namely, after division of the vagi, apnœa cannot obviously be due to such reflex action. In such depressed conditions of the respiratory centre, the blood becomes more venous than normal, and then the rapid inflation of the lungs with air will produce an apnœic condition. Fredericq still holds that ordinary apnœa has a chemical rather than a nervous origin. He attributes it, however, not to over-oxygenation, but to a lessening of the carbonic acid in the blood.

Special Respiratory Acts.

Coughing.—In the act of coughing there is first of all a deep inspiration, followed by an expiration; but the latter, instead of being easy and uninterrupted, as in normal breathing, is obstructed, the glottis being momentarily closed by the approximation of the vocal cords. The abdominal muscles, then strongly acting, push up the viscera against the diaphragm, and thus make pressure on the air in the lungs until its tension is sufficient to noisily open the vocal cords which oppose its outward passage. In this way considerable force is exercised, and mucus or any other matter that may need expulsion from the air-passages is quickly and sharply expelled by the outstreaming current of air. The act is a reflex one, the sensory surface which is excited being the mucous membrane of the larynx, and the superior laryngeal nerve is the afferent nerve; stimulation of other parts of the respiratory mucous membrane will also produce cough, and the point of bifurcation of the trachea is specially sensitive. Other sensory surfaces may also act as the "*signal surface*" for a cough. Thus, a cold draught on the skin, or tickling the external auditory meatus, in some people will set up a cough.

The question has been discussed whether such a thing as a stomach cough exists; it has not been produced experimentally, but there is no reason why irritation of the gastric mucous membrane, supplied as it is by the vagus, should not cause the reflex act of coughing.

Sneezing.—The same remarks that apply to coughing are almost exactly applicable to the act of sneezing; but, in this instance, the blast of air, on escaping from the lungs, is directed, by an instinctive contraction of the pillars of the fauces and descent of the soft palate, chiefly through the nose, and any offending matter is thence expelled.

The "signal surface" is usually the nasal mucous membrane, but here, as in coughing, other causes (such as a bright light) will sometimes set the reflex going.

Hiccough is an involuntary sudden contraction of the diaphragm, causing an inspiration which is suddenly arrested by the closure of the glottis, causing a characteristic sound. It arises from gastric irritation.

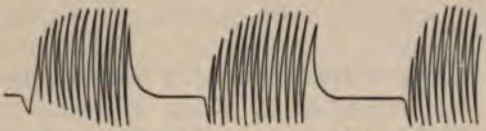

FIG. 332.—Cheyne-Stokes respiration. (After Waller.)

Snoring is due to vibration of the soft palate.

Sobbing consists of a series of convulsive inspirations at the moment of which the glottis is partially closed.

Sighing and Yawning are emotional forms of inspiration, the latter associated with stretching movements of jaws and limbs. They appear to be efforts of nature to correct, by an extra deep inspiration, the venosity of the blood due to inactivity produced by ennui or grief. Their contagious character is due to sympathy.

Among abnormal disturbances of the nervous mechanism of respiration, the following diseases must be mentioned: laryngismus stridulus, asthma, and whooping-cough.

Cheyne-Stokes respiration is due to rhythmical activity of the respiratory centre. It reminds one somewhat of the Traube-Hering waves due to a similar rhythmical activity of the vaso-motor centre. It is seen in many nervous diseases and in fatty degeneration of the heart. A typical tracing of the condition is given above (fig. 332). It is seen to a slight extent during ordinary sleep, and is very marked in hibernating animals.

Pembrey and Pitts have recently taken graphic records of this condition in the hibernating dormouse, hedgehog, marmot and bat. In some cases the respiration has the typical Cheyne-Stokes character, with a gradual waxing and waning (fig. 333). In other cases periods of respiratory activity alternate with periods of apnœa, but all the respiratory efforts are about equal in force. (Biot's respiration.)

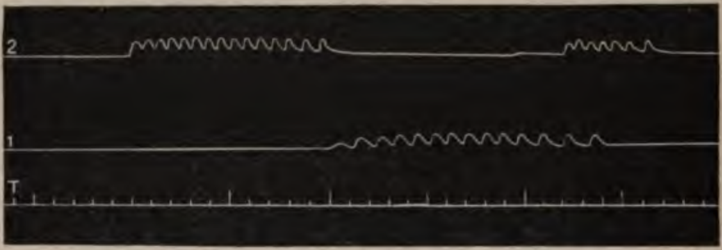

FIG. 333.—Cheyne-Stokes respiration in hibernating dormouse. The line marked T gives time in seconds Line 1 gives the tracing of a respiratory group which occurred once every 80 seconds, the temperature of the animal being 11° C. On warming the animal to 13° C. the respiratory groups became more frequent (line 2). On warming the animal still further it awakened, and breathing, at first accompanied by shivering, became continuous. (Pembrey and Pitts.)

The Effect of Respiration on the Circulation.

The main effect of respiration on the circulation is shown in the accompanying figure. It will be noticed that the arterial pressure rises with inspiration and falls with expiration, but that the two events are not quite synchronous, the rise of pressure beginning a

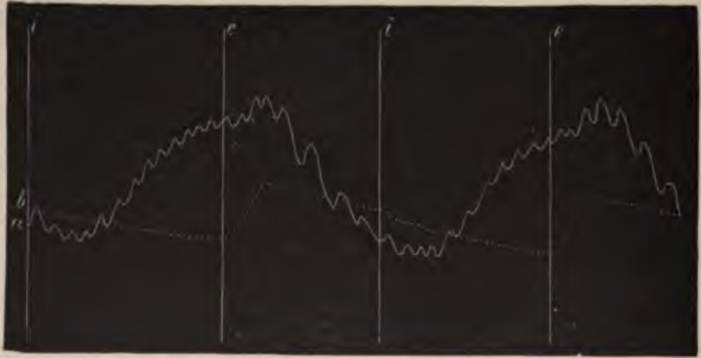

FIG. 334.—Comparison of blood-pressure curve with curve of intra-thoracic pressure. (To be read from left to right.) *a* is the curve of blood-pressure with its respiratory undulations, the slower beats on the descent being very marked; *b* is the curve of intra-thoracic pressure obtained by connecting one limb of a manometer with the pleural cavity. Inspiration begins at *i* and expiration at *e*. The intra-thoracic pressure rises very rapidly after the cessation of the inspiratory effort, and then slowly falls as the air issues from the chest; at the beginning of the inspiratory effort the fall becomes more rapid. (M. Foster.)

little later than the inspiratory act, and the fall a little later than the expiratory act.

It will also be seen that the heart beats more rapidly during the rise of blood-pressure than during the fall. This difference disappears when the vagi are cut. Respiratory undulations, however, are still present, though not so marked as before; hence the cardiac variations are not their sole cause. They are chiefly the result of the mechanical conditions dependent on the lungs and heart with its large vessels being contained within the air-tight thorax. When the capacity of the chest is increased in inspiration, the tension of the lung tissue due to its greater expansion is increased; hence the difference between the intra-pleural pressure, and that in the lungs (which is atmospheric) becomes more marked, for the difference of pressure is to be measured by the elastic force of the lung tending to produce its collapse. If the intra-thoracic pressure is measured, it is found that it varies from -5 to -7 mm. of mercury at the end of expiration to -30 at the end of a deep inspiration; that is to say, from 5 to 7 to 30 mm. less than the atmospheric pressure (760 mm. of mercury). The pressure outside the heart and large vessels is correspondingly diminished to the same extent, and produces its main effect (distension) upon the veins because they are never fully distended, and because the pressure within them is low. This increase in the "pressure gradient" (*i.e.*, the *rate* of fall of pressure) between the *intra* and *extra* thoracic great veins results in a proportionately more rapid flow of blood into the thorax, and therefore into the right side of the heart; for within certain limits the right heart can be easily expanded more fully if a greater supply of blood is provided. Consequently, the output from the right side increases, and thus *viâ* the pulmonary circuit the inflow into the left heart is increased; in its turn, therefore, the output from the left ventricle rises, and so the aortic pressure is raised. If the aorta and its branches within the thorax were as undistended as the veins and right auricle, this effect would be counteracted, but inasmuch as the aorta and arteries are thick-walled and already over-distended, an increased inflow into them must lead to a further distension, *i.e.*, a further rise of pressure. For we may altogether neglect the change in rate of flow along these vessels due to the change in pressure gradient, not because it is insufficient in itself to produce a distinct change in the flow, if the blood were free to move easily, but because the outflow from the arteries has to take place through a high peripheral resistance, and this small pressure change is not able to exert any appreciable effect in accelerating the flow through such a high peripheral resistance. We must note, too, that the change in pressure gradient would tend to decrease the outflow, not to increase it. The pressure gradient in arteries and in veins are about equal in magnitude, that in the veins being probably steeper than that in the large arteries. All these conditions are reversed when, with the expiratory act, the thorax returns to its former size, and the arterial blood-pressure falls in consequence.

The effect of inspiration on arterial blood-pressure is at first assisted by the pressure of the diaphragm as it descends on the abdominal veins, and blood is thus sent upwards into the chest by the vena cava inferior. On the other hand, this is to some extent counterbalanced by the obstruction in the passage of the blood downwards in the abdominal aorta, and upwards from the veins of the lower extremities, but again the veins are the vessels more easily influenced by moderate changes in external pressure.

We now come to the cause of the delay we have noted in the blood-pressure tracing in following the respiratory movements. One effect of the diminished intra-thoracic pressure which occurs during inspiration is an increase in the capacity of the pulmonary capillaries, and thus, though more blood is sent into the pulmonary circulation, the resulting increase in outflow is for a time delayed because the capacity of the pulmonary vessels has simultaneously become greater. As soon as this increase in capacity is satisfied, the accelerated flow from the right heart makes itself felt on the left side with the results already explained. In some animals, such as the rabbit, the rise of blood-pressure occurs during expiration, and the fall accompanies inspiration. This is simply because the rabbit is an animal which breathes very quickly; we have seen there is a delay in the inspiratory rise of pressure; if the animal breathes quickly enough, inspiration is over and expiration has begun before the rise of pressure occurs. By making the rabbit breathe slowly (Fredericq accomplished this by cooling the medulla oblongata), the tracing obtained is similar to that which is got from an animal like a dog, which normally breathes slowly.

When the chest of an animal is freely opened, and artificial respiration performed in order to keep it alive, respiratory undulations on the arterial pressure curve are still seen, but they are in the reverse direction. These obviously cannot be produced in the mechanical way just described. The forcible inflation with air at first squeezes more blood out of the alveolar capillaries, that is, the capacity of these vessels is diminished, and this temporarily increases the quantity of blood thrown into the left ventricle, and so causes a rise of arterial pressure. But the increased intra-alveolar pressure has also been shown to lead to an increased resistance to the pulmonary circulation, and the rate of flow into the left side consequently falls; the aortic pressure therefore falls; while the pressure in the pulmonary artery rises. If the high positive intra-pulmonary air-pressure persisted, a condition would soon be reached, in which the increased blood-pressure in the pulmonary artery would lead to a greater flow, and the aortic blood-pressure would remain constant; this, however, has been shown to take a much longer time than an ordinary respiration period. Hence the main effect of inflations of the lungs at the ordinary respiration rate is to diminish the aortic blood-pressure; this rises again for the opposite reasons, in the intervals of deflation, which correspond to expiration.

If artificial respiration is performed while the thorax is not opened, a further complication arises from the fact that the increased intrapleural pressure decreases the rate of flow of blood into the thorax, and under these conditions the blood-pressure in the pulmonary artery falls, and in consequence the fall in the aortic blood-pressure becomes more marked with each inflation than it does when the thorax is open.

The last point of detail we have to consider is the cause of the greater frequency of the heart during the inspiratory phase, a phenomenon which is evidently due to lessening of vagus action, since the inequality of the heart rate disappears when the vagi are cut. The question before us is, What is the cause of the rhythm in the activity of the vagus centre? There appear to be two factors concerned in its causation: one is a reflex action, the other is what may be termed a central overflow. We will consider these separately.

1. *The reflex.* Stimulation of the pulmonary branches of the vagus by electrical stimuli, or of their terminations in the alveoli by certain irritating vapours like bromine, causes a reflex inhibition of the heart; great distension of the alveoli has a similar effect, but moderate distension, such as occurs in an ordinary inspiration, has the opposite reflex effect, causing the heart to beat more rapidly. The afferent fibres from the pulmonary alveoli enter the bulb by the upper set of the rootlets of the combined glossopharyngeal-vagus-spinal accessory nucleus (the *a* group, p. 247). Sometimes the rootlets of this group are three in number, sometimes two. When there are two, the lower rootlet, when there are three the lower two rootlets, contain the fibres in question (Cadman).

2. *The overflow.* The respiratory centre exhibits alternate phases of activity, or what is termed a rhythmical action. It is in close anatomical connection with two other important centres in the bulb, namely, the cardio-inhibitory and the vaso-motor centres. Considering how closely these three centres are connected by association fibres, it is not surprising that the cells of the two latter centres should be affected by the rhythm of the cells of the respiratory centre, and the term overflow is an expression that roughly indicates what occurs. This overflow from the respiratory centre affects its two neighbours in the same way. During inspiration the activity of both the cardio-inhibitory centre and of the vaso-motor centre is diminished, hence the heart beats faster. The factor which we have

termed the overflow is more important than that which we have described as the reflex.

These facts show us that the parallelism of the respiratory and arterial pressure curves is not merely the result of the mechanical conditions already described, though these are the most important. But in the normal condition with the thorax closed, and the vagi uncut, certain nervous factors come also into play. During inspiration these are:—

1. A reflex from the terminations of the vagi in the pulmonary alveoli, which produces a lessening of vagus action, and so quickening of the heart.

2. An overflow from the respiratory to the cardio-inhibitory centre, which is still more powerful in producing the same effect.

3. An overflow from the respiratory to the vaso-motor centre, which produces decreased constriction of the systemic arterioles. By itself the third nervous factor would lessen arterial pressure, but in conjunction with the other two, and in conjunction also with the mechanical conditions described, the main result is a rise of arterial pressure during inspiration.

Valsalva's Experiment.—In speaking of the effects of expiration, we have considered only ordinary quiet expiration. With forced expiration, there is considerable impediment to the circulation; this is markedly seen in what is called Valsalva's experiment. This consists in making a forced expiratory effort with the mouth and nose shut; the effects are most marked in people with an easily compressible thorax. By such an act the intrathoracic and abdominal pressures rise so greatly that the outlets of the veins of the limbs, head, and neck into the thorax are blocked. At first, the blood in the abdominal veins is drawn on into the right heart; this produces a slight rise of arterial pressure; but soon, if the effort is continued, the lungs are emptied of blood, the filling of the right heart is opposed, and the blood is dammed back in the peripheral veins, where the pressure rises to mean arterial pressure. The arterial pressure begins then to fall; but before any considerable fall occurs, the expiratory effort ceases from exhaustion of the subject of the experiment, and a deep inspiration is taken. During this inspiration, the blood delivered by the right heart is all used in the filling of the dilated and comparatively empty pulmonary vessels; thus several beats of the left ventricle become abortive, and produce no effect on the radial artery; the face blanches, and the subject becomes faint from cerebral anæmia.

Asphyxia.

Asphyxia may be produced in various ways: for example, by the prevention of the due entry of oxygen into the blood, either by direct obstruction of the trachea or other part of the respiratory passages, or by introducing instead of ordinary air a gas devoid of oxygen, or by interference with the due interchange of gases between the air and the blood.

The symptoms of asphyxia may be roughly divided into three stages: (1) the stage of exaggerated breathing; (2) the stage of convulsions; (3) the stage of exhaustion.

In the *first stage* the breathing becomes more rapid, and at the same time deeper than usual, inspiration at first being especially exaggerated and prolonged. The muscles of extraordinary inspiration are called into action, and the effort to respire is laboured and painful. This is soon followed by a similar increase in the expiratory efforts, which become excessively prolonged, being aided by all the muscles of extraordinary expiration. During this stage, which lasts a varying time from a minute upwards, according as the deprivation of oxygen is sudden or gradual, the lips become blue, the eyes are prominent, and the expression intensely anxious. The prolonged respirations are accompanied by a distinctly audible sound; the muscles attached to the chest stand out as distinct cords. This stage includes the two conditions *hyperpnœa* (excessive breathing) and *dyspnœa* (difficult breathing), which follows later. It is due to the increasingly powerful stimulation of the respiratory centre by the increasingly venous blood.

In the *second stage*, which is not marked by any distinct line of demarcation from the first, the violent expiratory efforts become convulsive, and then give way, in men and other warm-blooded animals, to general convulsions, which arise from the further stimulation of the centres in brain and cord by venous blood. Spasms of the muscles of the body in general occur, and not of the respiratory muscles only. The convulsive stage is a short one, and lasts less than a minute.

The *third stage*, or stage of *exhaustion*. In it the respirations all but cease, the spasms give way to flaccidity of the muscles, there is insensibility, the conjunctivæ are insensitive and the pupils are widely dilated. Every now and then a prolonged sighing inspiration takes place, at longer and longer intervals, until breathing ceases altogether, and death ensues. During this stage the pulse is scarcely to be felt, but the heart may beat for some seconds after the respiration has stopped. The condition is due to the gradual paralysis of the centres by the prolonged action of the venous blood. This stage may last three minutes and upwards.

After death from asphyxia it is found in the great majority of cases that the right side of the heart, the pulmonary arteries, and the systemic veins are gorged with dark, almost black, blood, and the left side of the heart, the pulmonary veins, and the arteries are empty. The explanation of these appearances may be thus summarised: when oxygenation ceases, venous blood at first passes freely through the lungs to the left heart, and so to the great arteries.

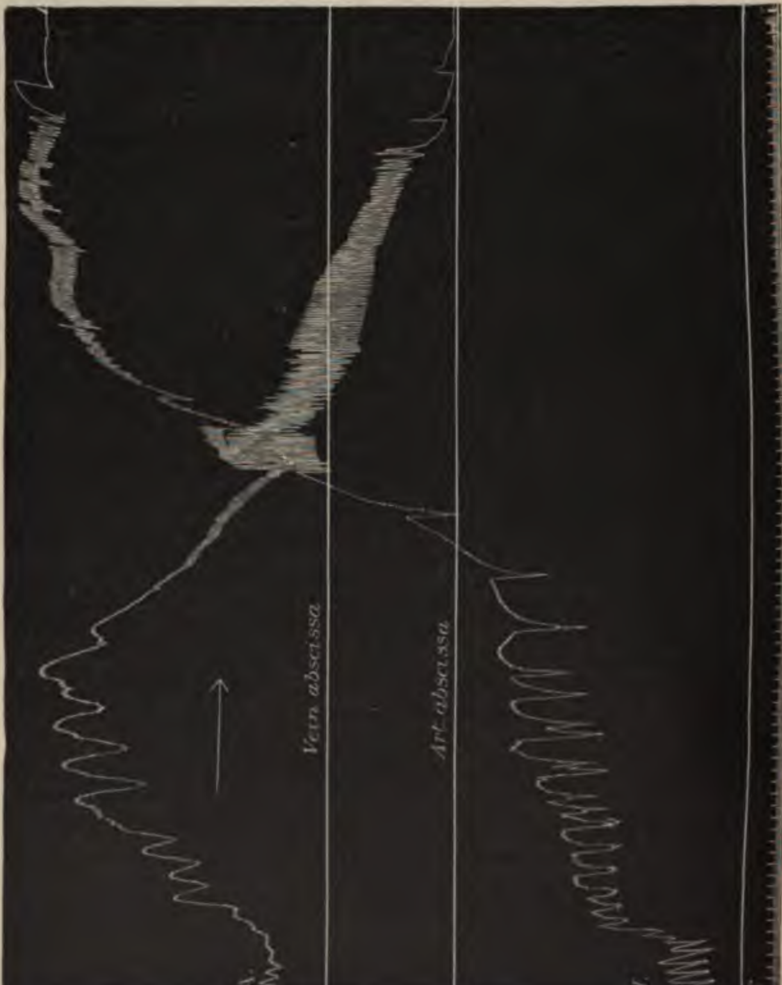

FIG. 335.—Tracing of asphyxia from a curarised cat; artificial respiration ceased at about the third time marking from the left. The upper tracing (A) is that of the arterial pressure, taken with a mercurial manometer. The lower tracing (V) which at first indicates negative pressure is that of the venous tension taken with C. J. Martin's salt solution manometer.

Owing to the stimulation of the vaso-motor centres, by the venous blood, the arterioles, particularly those of the splanchnic area, are constricted; the arterial blood-pressure therefore rises, and the left side of the heart becomes distended. The highly venous blood passes through the arterioles, and, favoured by the laboured respiratory movements, arrives at the right side of the heart, which it fills and distends; the right side of the heart is becoming feebler at the same time, and therefore unable to effectively discharge its blood through the pulmonary circuit. Simultaneously the left ventricle is also becoming weakened, and therefore its suction action diminishes. In this way the blood is dammed back in the right heart and veins. In the third stage of asphyxia, the left side of the heart therefore gets into the empty condition in which it is found after death. Some consider that the early onset of rigor mortis in the left ventricle may be in part a cause of its contracted and empty condition.

In the first and second stages of asphyxia, the arterial pressure rises until it reaches a point far above the normal; this is due to the constriction of the arterioles. The fall of pressure in the last stage is mainly due to heart failure. If the vagi are not divided previously, the rise of pressure is much less, and the heart beats very slowly: this enables the heart to last longer, and is due to excitation of the cardio-inhibitory centre by venous blood. The accompanying photograph of a tracing, which I owe to Prof. C. J. Martin, shows these effects; it has been somewhat reduced in size for purposes of reproduction. The lower tracing is that of venous pressure taken with a salt solution manometer from the jugular vein. It will be noticed that the fall of arterial pressure in the last stage is accompanied with a great rise of venous pressure due to the venous congestion just described.

Effects of Breathing Gases other than the Atmosphere.

The diminution of oxygen has a less direct influence in the production of asphyxia than the increased amount of carbonic acid. Nevertheless, the fatal effect of **carbonic acid** in the blood when a due supply of oxygen is maintained, resembles rather the action of a narcotic poison than it does asphyxia.

Then, again, we must carefully distinguish the asphyxiating effect of an insufficient supply of oxygen from the directly poisonous action of such a gas as **carbonic oxide**, which is contained to a considerable amount in common coal-gas. The fatal effects often produced by this gas (as in accidents from burning charcoal stoves in small, close rooms) are due to its entering into combination with the hæmoglobin of the blood-corpuscles, and thus expelling the oxygen. **Hydrogen** may take the place of nitrogen if the oxygen is in the usual proportion, with no marked ill effect. **Sulphuretted hydrogen** interferes with the oxygenation of blood. **Nitrous oxide** acts directly on the nervous system as a narcotic. Certain gases, such as **carbon dioxide** in more than a certain proportion; **sulphurous and other acid gases, ammonia**, and **chlorine** produce spasmodic closure of the glottis, and are irrespirable.

Alterations in the Atmospheric Pressure.

The normal condition of breathing is that the oxygen of the air breathed should be at the pressure of ⅕ of the atmosphere, viz., ⅕ of 760 mm. of mercury, or 152 mm., but considerable variations may occur without producing ill effects. This is due to the fact that the blood gases are mostly in a state of chemical combination, not of simple solution. Variations beyond certain limits are, however, fatal. When the tension of oxygen exceeds 3½ atmospheres (*i.e.*, in air at a pressure of 17 atmospheres), slow but powerful poisonous (narcotic) effects are produced on all living matter. (Bert.) The excised sartorius is paralysed by about half an hour's exposure to 80 atmospheres of oxygen; and the excised frog's heart ceases to beat in about two hours under the same conditions. It is dangerous for men to work in caissons where the atmospheric pressure is greater than 4 atmospheres. Even lower pressures may be followed on "decompression" (*i.e.*, on coming out of the increased pressure), by what are called "bends," that is, pains in the joints and muscles by paralysis, and auditory symptoms such as deafness and vertigo. The cause of such symptoms is probably the setting free of bubbles of nitrogen in the lymph spaces and capillaries; any oxygen set free is rapidly re-absorbed by the blood. Capillary embolism from gas bubbles in the central nervous system is the most probable cause of the paralysis. (Bert.) Oxygen poisoning may be a secondary cause of the symptoms. Short shifts are essential for caisson workers, for then the body has not time to become saturated with gas at the caisson pressure. Decompression must also be gradual and slow.

A toad was but slightly effected by 5 minutes' exposure to 20 atmospheres of oxygen, but after 40 minutes on "decompression" it went into tetanic convulsions and died; the heart was distended with frothed blood; bubbles of gas were in all the lymph spaces, in the anterior chamber of the eye, and other parts. A mouse in a similar high pressure is narcotised, and on "decompression" convulsions and death ensue. (L. Hill.) Prolonged exposure to 2 atmospheres of oxygen is followed by pneumonia. (Lorrain Smith.) Mechanical pressure by itself has little or no influence; thus frog's muscle is not injured by exposure to fluid pressure in salt solution equal to 400 atmospheres. Crustacea are found alive on marine telegraph cables at a depth where the pressure is as great.

Turning now to diminution of pressure, we find that "mountain sickness" occurs at the height of 4800 metres, the summit of Mt. Blanc. Here the pressure of oxygen is only 11·53 per cent. of an atmosphere. The malady is increased by muscular effort, and is due to want of oxygen. In those who habitually live in high altitudes, the number of red blood-corpuscles is increased. Crocé-Spinelli, the balloonist, perished at an altitude of 8600 metres, where the tension of oxygen would be 7 per cent. of an atmosphere. His companion Tissandier recovered. In such cases muscular paralysis occurs before loss of consciousness. Higher ascents could be made by aeronauts if they breathed oxygen from a gas cylinder. (Bert.) That death is due to want of oxygen and not to the setting free of gas bubbles in the blood is shown by the following fact: a sparrow lived in pure oxygen at 95 mm. of mercury pressure. Haldane has shown that animals can live in two atmospheres of oxygen after all the hæmoglobin is taken up by carbonic oxide, for then sufficient oxygen is dissolved in the blood-plasma.

CHEMISTRY OF RESPIRATION.

The air in the air vesicles and the blood in the capillaries are separated only by the thin capillary and alveolar walls. The blood parts with its excess of carbonic acid and watery vapour to the alveolar air; the blood at the same time receives from the alveolar air a supply of oxygen which renders it arterial.

The intake of oxygen is the commencement, and the output of carbonic acid is the end of the series of changes known as respiration. The gaseous interchange in the lungs is often called *external respiration.* The actual combustion processes take place all over the body and constitute what is known as *internal* or *tissue-respiration.* The oxygen which goes into the blood is held there in loose combination as oxyhæmoglobin. In the tissues this substance parts with its respiratory oxygen. The oxygen does not necessarily undergo immediate union with carbon to form carbonic acid, and with hydrogen to form water, but in most cases as in muscle, is held in reserve by the tissue itself. Owing to this reserve oxygen, a muscle will contract in an atmosphere of pure nitrogen and yet give off carbonic acid; and a frog will live under the same conditions and give off carbonic acid for several hours. Besides carbonic acid and water, certain other products of combustion are generated; those like urea and uric acid, which are the result of nitrogenous metabolism, ultimately leave the body in the urine. The carbonic acid and a portion of the water find an outlet by the lungs.

Inspired and Expired Air.—The composition of the inspired or atmospheric air and the expired air may be compared in the following table:—

	Inspired air.	Expired air.
Oxygen . . .	20·96 vols. per cent.	16·03 vols. per cent.
Nitrogen . .	79 ,, ,,	79 ,, ,,
Carbonic acid .	0·04 ,, ,,	4·4 ,, ,,
Watery vapour .	variable	saturated
Temperature . .	,,	that of body (37° C.)

The nitrogen remains unchanged. The recently discovered gases argon, crypton, etc., are in the above table reckoned in with the nitrogen. They are, however, only present in minute quantities. The chief change is in the proportion of oxygen and carbonic acid. The loss of oxygen is about 5, the gain in carbonic acid about 4·5. If the inspired and expired airs are carefully measured at the same temperature and barometric pressure, the volume of expired air is thus found to be rather less than that of the inspired.* The conversion of oxygen into carbonic acid would not cause any change in the volume of the gas; for a molecule of oxygen (O_2) would give rise to a molecule of carbonic acid (CO_2) which would occupy the same volume (Avogadro's law). It must, however, be remembered that carbon is not the only element which is oxidised. Fat and proteid contain a number of atoms of hydrogen, which, during metabolism, are oxidised to form water; a small amount of oxygen is also used in the formation of urea. Carbohydrates contain sufficient oxygen in their own molecules to oxidise their hydrogen; hence the apparent loss of oxygen is least when a vegetable diet (that is, one consisting largely of starch and other carbohydrates) is taken, and greatest when much fat and proteid are eaten. The quotient $\frac{CO_2 \text{ given off}}{O_2 \text{ absorbed}}$ is called the ***respiratory quotient.*** Normally it is $\frac{4\cdot5}{5} = 0\cdot9$, but it varies considerably with diet as just stated. It varies also with muscular exercise as the output of carbonic acid is then increased both absolutely and relatively to the amount of oxygen used up.

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* This diminution of volume will cause a slight rise in the proportionate volume of nitrogen per cent.

The amount of respiratory interchange of gases is estimated by enclosing an animal in an air-tight chamber, except that there is a tube entering and another leaving it; by one tube oxygen or air can enter, and is measured by a gas-meter as it passes in. The air is drawn through the chamber, and leaves it by the other tube; this air has been altered by the respiration of the animal, and in it the carbonic acid and water are estimated; the carbonic acid is estimated by drawing the air through tubes containing a known amount of an alkali; this combines with the carbonic acid and is increased in weight: the increase in weight gives the amount of carbonic acid; the alkali used in Regnault and Reiset's apparatus was potash; Pettenkofer used baryta water; Haldane recommends soda-lime. The water is estimated in tubes containing pumice moistened with sulphuric acid.

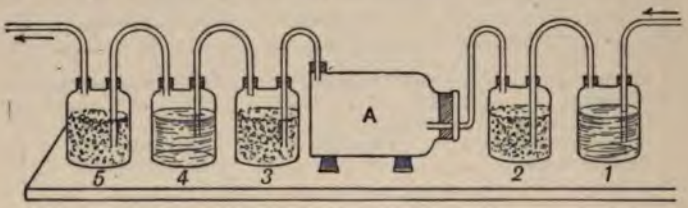


FIG. 336.—Haldane's apparatus for estimating the carbonic acid and aqueous vapour given off by an animal.

The accompanying drawing (fig. 336) shows the essential part of the simple but effective apparatus used by Haldane. The animal is placed in the vessel A; air is sucked through the apparatus (which must be perfectly air-tight) by a water pump at a suitable rate. The arrows indicate the direction in which the air passes. It goes first through two Woulff's bottles, 1 and 2. No. 1 contains soda-lime, which frees the air from carbonic acid; No. 2 contains pumice-stone moistened with sulphuric acid, which frees the air from aqueous vapour. The air next reaches the animal chamber, and the animal gives off to it carbonic acid and aqueous vapour. It passes then through the three bottles, 3, 4, and 5. No. 3 contains pumice and sulphuric acid, which removes the water; No. 4 contains soda-lime, which absorbs the carbonic acid; and No. 5 contains pumice and sulphuric acid, which absorbs any water carried over from bottle 4. The increase of weight in bottle 3 at the end of a given time (*e.g.*, an hour) is the weight of water given off by the animal in that time; the increase of weight in bottles 4 and 5 weighed together gives the amount of carbonic acid produced by the animal in the same time.

Ranke gives the following numbers from experiments made on a man, who was taking a mixed diet consisting of 100 grammes of proteid, 100 of fat, and 250 of carbohydrate in the twenty-four hours. The amount of oxygen absorbed in the same time was 666 grammes; of which 560 passed off as carbonic acid, 9 in urea, 19 as water formed from the hydrogen of the proteid, and 78 from that of the fat.

Vierordt from a number of experiments on human beings gives the following numbers: the amount of oxygen absorbed in the twenty-four hours, 744 grammes; this leads to the formation of 900 grammes of carbonic acid (this contains about half a pound of carbon) and 360 grammes of water.

The respiratory interchange is lessened during sleep. It is especially small in the winter sleep of hibernating animals.

Circumstances affecting the amount of carbonic acid excreted. (a) *Age and sex.* In males the quantity increases with growth till the age of 30; at 50 it begins to diminish again. In females the decrease begins when menstruation ceases. In females the quantity exhaled is always less than in males of the same age.

(b) *Respiratory movements.*—The quicker the respiration the smaller is the proportionate quantity of carbonic acid in each volume of expired air. The total quantity is, however, increased, not because more is formed in the tissues, but more is got rid of. The last portion of the expired air which comes from the more remote parts of the lungs is the richest in carbonic acid.

(c) *External temperature.*—In cold-blooded animals, a rise in the external temperature causes a rise in their body temperature, accompanied with increased chemical changes, including the formation of a larger amount of carbonic acid. In warm-blooded animals, it is just the reverse; in cold weather the body temperature has to be kept at the normal level, and so increased combustion is necessary.

(d) *Food.*—This produces an increase which usually comes on about an hour after a meal.

(e) *Exercise.*—Moderate exercise causes an increase of about 30 to 40 per cent. in the amount excreted. With excessive work, the increase is still greater.

Diffusion of Gases within the Lungs.—If two chambers containing a mixture of gases in unequal amount are connected together, a slow movement called diffusion takes place until the percentage amount of each gas in each chamber is the same. Let us suppose that one chamber contains a large quantity of oxygen and a small quantity of carbonic acid; and the other a small quantity of oxygen and a large quantity of carbonic acid; the oxygen moves from the first to the second, and the carbonic acid from the second to the first chamber. The pressure of a gas is proportional to the percentage amount in which it is present in a mixture. This is true for each gas in a mixture, the presence of the others making no difference.

In the atmosphere, for instance, the total barometric pressure is 760 mm. of mercury; the amount of oxygen in the air is roughly one-fifth, and the pressure it exercises is also one-fifth of 760; the nitrogen accounts for the other four-fifths. The carbonic acid is present in such small quantities that the pressure it exercises is only a fraction of a millimetre.

In the alveolar air (which can be obtained by catheterisation) the carbonic acid is present in larger and the oxygen in smaller amount; and in the intermediate air passages there is an intermediate condition: hence, as in the two chambers we first considered, oxygen diffuses down to the air vesicles, and carbonic acid from them. These movements are, however, by themselves too slow to be efficient, and are assisted by the large draughts which are created in the respiratory tract by the respiratory movements of the chest.

Catheterisation of the lungs.—In animals determinations of the composition of the alveolar air have been made in an occluded portion of the lung by Pflüger's lung catheter. This consists of a fine elastic catheter surrounded by a tube with an enlargement towards the free end. It is introduced through the dog's trachea into a bronchus, and it must be small enough to allow air to pass freely to other parts of the lung. The rubber enlargement is then inflated; this shuts off a portion of the lung, from which the alveolar air is then withdrawn by the inner tube. In such experiments, the alveolar air was found to contain 3·5 per cent. of carbon dioxide, whereas the expired air contained 2·8 per cent. The number 3·5 is higher than normal, for under the conditions of the experiment it was undiluted with any tidal air. Analysis of the air so obtained gives its composition after an equilibrium has been set up with the gases of the blood, which is passing through the occluded portion of the lung.

Gases of the Blood.—From 100 volumes of blood, about 60 volumes of gas can be removed by the mercurial air-pump. The average composition of this gas in dog's blood is:—

	Arterial blood.	Venous blood.
Oxygen	20	8 to 12
Nitrogen	1 to 2	1 to 2
Carbonic acid	40	46

The nitrogen in the blood is simply dissolved from the air just as water would dissolve it; it has no physiological importance. The other two gases are present in much greater amount than can be explained by simple solution; they are, in fact, chiefly present in loose chemical combinations. Less than one volume of the oxygen and about two of carbonic acid are present in simple solution in the plasma.

Oxygen in the Blood.—The amount of gas dissolved in a liquid varies with the pressure of the gas; double the pressure and the amount of gas dissolved is doubled. The oxygen of the blood does not vary directly with oxygen pressure, for the amount of that gas in simple solution forms only a small fraction of the total present. This small amount is of course doubled by doubling the pressure, but such an increase is insignificant, the bulk of the oxygen being in chemical union with hæmoglobin. The oxygen of oxyhæmoglobin can be replaced by equivalent quantities of other gases like carbonic oxide. The tension or partial pressure of oxygen in the air of the alveoli is less than that in the atmosphere, but greater than that in venous blood; hence oxygen passes from the alveolar air into the blood-plasma; the oxygen immediately combines with the hæmoglobin, and thus leaves the plasma free to absorb more oxygen; and this goes on until the hæmoglobin is entirely, or almost entirely, saturated with oxygen. The reverse change occurs in the tissues when the partial pressure of oxygen is lower than in the plasma, or in the lymph that bathes the tissue elements; the plasma parts with its oxygen to the lymph, the lymph to the tissues; the oxyhæmoglobin then undergoes dissociation to supply more oxygen to the plasma and lymph, and thus in turn to the tissues once more. This goes on until the oxyhæmoglobin loses a great portion of its store of oxygen, but even in asphyxia it does not lose all.

The following values are given by Fredericq for the tension of oxygen in percentages of an atmosphere. His experiments were made on dogs.

External air	20·96	↓
Alveolar air	18	
Arterial blood	14	
Tissues	0	

The arrow shows the direction in which the gas passes.

When the gases are being pumped off from the blood, very little oxygen comes off till the pressure has been greatly reduced, and then, at a certain point, it is disengaged at a burst. This shows that it is not in simple solution but is united chemically to some constituent of the blood, which is suddenly dissociated at the reduced pressure. This constituent of the blood is hæmoglobin.

The avidity of the tissues for oxygen is shown by Ehrlich's experiments with methylene blue and similar pigments. Methylene blue is more stable than oxyhæmoglobin; but if it is injected into the circulation of a living animal, and the animal killed a few minutes later, the blood is found dark blue, but the organs (especially those which like glandular organs are in a state of activity) colourless. On exposure to oxygen the organs become blue. In other words, the tissues have removed the oxygen from methylene blue to form a colourless reduction product; on exposure to the air this once more unites with oxygen to form methylene blue.

Carbonic Acid in the Blood.—What has been said for oxygen holds good in the reverse direction for carbonic acid. Compounds are formed in the tissues where the tension of the gas is high: these pass into the lymph, then into the blood, and in the lungs they undergo dissociation, carbonic acid passing into the alveolar air, where the tension of the gas is comparatively low, though it is greater here than in the expired air.

The relations of this gas and the compounds it forms are more complex than in the case of oxygen. If blood is divided into plasma and corpuscles, it will be found that both yield carbonic acid, but the yield from the plasma is the greater. If we place blood in a vacuum it bubbles, and gives out all its gases; addition of a weak acid causes no further liberation of carbonic acid. When plasma or serum is similarly treated the gas also comes off, but about 5 per cent. of the carbonic acid is fixed—that is, it requires the addition of some stronger acid, like phosphoric acid, to displace it. Fresh red corpuscles will, however, take the place of the phosphoric acid, and thus it has been surmised that oxyhæmoglobin has the properties of an acid.

One hundred volumes of venous blood contain forty-six volumes of carbonic acid. Whether this is in solution or in chemical combination is determined by ascertaining the tension of the gas in the blood. One hundred volumes of blood-plasma would dissolve more than an equal volume of the gas at atmospheric pressure, if its solubility in plasma were equal to that in water. If, then, the carbonic acid were in a state of solution, its tension would be very high, but it proves to be only equal to 5 per cent. of an atmosphere. This means that when venous blood is brought into an atmosphere containing 5 per cent. of carbonic acid, the blood neither gives off any carbonic acid nor takes up any from that atmosphere. The instrument used in such determinations is called an aërotonometer (see p. 381). Hence the remainder of the gas, 95 per cent., is in a condition of chemical combination. The chief compound appears to be sodium bicarbonate.

The carbonic acid and phosphoric acid of the blood are in a state of constant struggle for the possession of the sodium. The salts formed by these two acids depend on their relative masses. If carbonic acid is in excess, we get sodium carbonate (Na_2CO_3), and mono-sodium phosphate (NaH_2PO_4); but if the carbonic acid is diminished, the phosphoric acid obtains the greater share of sodium to form disodium phosphate (Na_2HPO_4). In this way, as soon as the amount of free carbonic acid diminishes, as in the lungs, the amount of carbonic acid in combination also decreases; whereas in the tissues, where the tension of the gas is highest, a large amount is taken up into the blood, where it forms sodium bicarbonate.

The tension of the carbonic acid in the tissues is high, but one cannot give exact figures; we can measure the tension of the gas in certain secretions: in the urine it is 9, in the bile 7 per cent. The tension in the cells themselves must be higher still.

The following figures (from Fredericq) give the tension of carbonic dioxide in percentages of an atmosphere:—

Tissues	5 to 9	in dog.	↓
Venous blood	3·8 to 5·4		
Alveolar air	2·8		
External air	0·03		

The arrow indicates the direction in which the gas passes, namely, in the direction of pressure from the tissues to the atmosphere.

In some other experiments, also on dogs, the following are the figures given:—

Arterial blood	2·8	↓
Venous blood	5·4	
Alveolar air	3·56	
Expired air	2·8	

It will be seen from these figures that the tension of carbonic acid in the venous blood (5·4) is higher than in the alveolar air (3·56); its passage into the alveolar air is therefore intelligible by the laws of diffusion. Diffusion, however, should cease when the tension of the gas in the blood and alveolar air are equal. But the transference goes beyond the establishment of such an equilibrium, for the tension of the gas in the blood continues to sink until it is ultimately less (2·8) than in the alveolar air.

The whole question is beset with great difficulties and contradictions. Analyses by different observers have given very different results, but if such figures as those just quoted are ultimately found to be correct, we can only explain this apparent reversal of a law of nature by supposing with Bohr that the alveolar epithelium possesses the power of excreting carbonic acid, just as the cells of secreting glands are able to select certain materials from the blood and reject others. Recent work by Bohr and Haldane has also shown that in all probability the same explanation—epithelial activity—must be called in to account for the absorption of oxygen. In the swim-bladder of fishes (which is analogous to the lungs of mammals) the oxygen is certainly far in excess of anything that can be explained by mere diffusion. The storage of oxygen, moreover, ceases when the vagus nerves which supply the swim-bladder are divided.

The Aërotonometer.—This instrument was invented by Pflüger, and of the modifications that have been introduced since then, that of Fredericq is the simplest. It merely consists of a long glass tube surrounded by a water-jacket at body temperature. The tube is filled with a known mixture of gases, and the blood from the carotid artery is allowed to slowly trickle down the tube; the blood then returns to the jugular vein. In order that the experiment may be continued for an hour or more, the animal's blood must be rendered incoagulable; this may be done by a previous injection of "peptone." This has the disadvantage of lowering the carbonic acid tension of the blood. Another way of rendering the blood incoagulable is to collect it, defibrinate it, and then return it to the circulation. The last step in the experiment consists in examining the composition of the gases left in the tube. The principle upon which the instrument rests is this:—If blood is brought into contact with a mixture of oxygen, nitrogen, and carbonic acid gas, it gives off some of its gases if their partial pressure is greater in the blood than the respective tensions of the gases in the mixture; if, on the other hand, the tension is lower in the blood than in the mixture for any gas or gases, they pass from the mixture to the blood. These interchanges go on until equilibrium is established. For example, suppose the aërotonometer contains at the start 10 per cent. of oxygen, 5 of carbonic acid, and 85 of nitrogen. Blood is then passed through it for an hour, and the gases are again analysed, and the mixture then contains 14 per cent. of oxygen, 2·8 of carbon dioxide, and the rest nitrogen; the tension of oxygen and carbon dioxide in the blood will then respectively be 14 and 2·8 per cent. of an atmosphere.

The Carbonic Oxide Method of Estimating the Oxygen Tension of Arterial Blood.—This method was devised by Haldane, and is considered by him and Lorrain Smith to give more trustworthy results than those obtained by the aërotonometer. If blood is exposed to a mixture of carbonic oxide and oxygen, the hæmoglobin will become saturated by these gases according to their relative tensions. If a number of experiments are performed using different percentages of carbonic oxide, the results may be expressed graphically as the curve of dissociation of carboxyhæmoglobin in air. When in place of such experiments *in vitro*, an animal is made to breathe air containing a known percentage of carbonic oxide, the comparison of the saturation of its blood with the saturation of its blood *in vitro* exposed to the same percentage of carbonic oxide in air (which has an oxygen tension of 20·9 per cent.) gives us the means of discovering the oxygen tension in the arterial blood of the lung capillaries; this will be higher or lower than that of the air according as the saturation by carbonic oxide is correspondingly lower or higher. A small animal like a mouse is made to breathe air containing a known percentage of carbonic oxide. After a sufficient time the animal is killed and the amount of carboxyhæmoglobin is determined colorimetrically in a drop of its blood. The data thus obtained are compared with the data previously expressed in the curve of dissociation of carboxyhæmoglobin in air; it is then easy to calculate whether the oxygen tension in the blood is higher or lower than that of air. The results of the method show generally that the tension of oxygen in the arterial blood as it leaves the lungs is higher than could result from simple diffusion of the oxygen through the alveolar epithelium; in other words the epithelial cells are capable of secreting oxygen into the blood until an oxygen-pressure is reached considerably above that in the alveolar air.

The results expressed in percentages of an atmosphere are as follows:—

Oxygen tension of arterial blood in man, 38·5; in mouse, 22·6; in dog, 21; in cat, 35·3; in rabbit, 27·6, and in birds, 30 to 50 per cent. The results in the case of man and larger animals probably require revision, as it is not certain that the time allowed for the establishment of the balance of carbonic oxide and oxygen has been sufficient in any of the experiments.

Tissue Respiration.—Before the processes of respiration were fully understood the lungs were looked upon as the seat of combustion; they were regarded as the stove for the rest of the body to which effete material was brought by the venous blood to be burnt up. When it was shown that the venous blood going to the lungs already contained carbonic acid, and that the temperature of the lungs is not higher than that of the rest of the body, this explanation had of necessity to be dropped.

Physiologists next transferred the seat of combustion to the blood; but since then numerous facts and experiments have demonstrated that it is in the tissues themselves, and not in the blood, that combustion occurs. The methylene-blue experiments already described

(p. 379) show this; and the following experiment is also quite conclusive. A frog can be kept alive for some time after salt solution is substituted for its blood. The metabolism goes on actively if the animal is kept in pure oxygen. The taking up of oxygen and giving out of carbonic acid must therefore occur in the tissues, as the animal has no blood.

Ventilation.—It is necessary to allude in conclusion to this very important practical outcome of our consideration of respiration.

Some Continental observers have stated that certain noxious substances are ordinarily contained in expired air which are much more poisonous than carbonic acid, but researches in this country have failed to substantiate this. If precautions be taken by absolute cleanliness to prevent admixture of the air with exhalations from skin, teeth, and clothes, the expired air only contains one noxious substance, and that is carbonic acid.

Absolute cleanliness is, however, not the rule; and the air of rooms becomes stuffy when the amount of expired air in them is just so much as to raise the percentage of carbonic acid to 0·1 per cent. An adult gives off about 0·6 cubic feet of carbonic acid per hour, and if he is supplied with 1000 cubic feet of fresh air per hour he will add 0·6 to the 0·4 cubic feet of carbonic acid it already contains; in other words, the percentage of that gas will be raised to 0·1. An hourly supply of 2000 cubic feet of fresh air will lower the percentage of carbonic acid to 0·07, and of 3000 cubic feet to 0·06, and this is the supply which is usually recommended. In order that the air may be renewed without giving rise to draughts, each adult should be allotted sufficient space in a room, at least 1000 cubic feet.

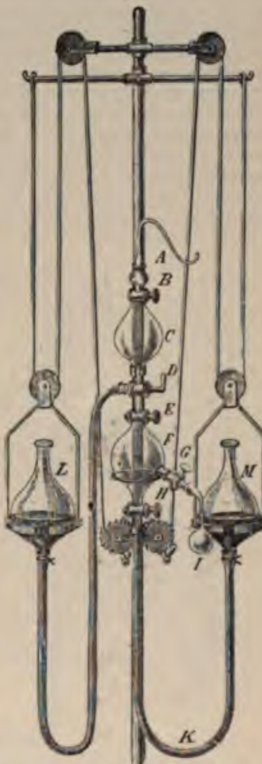


Fig. 337.—Ludwig's Mercurial Pump.

The Mercurial Air-Pump.

The extraction of the gases from the blood is accomplished by means of a mercurial air-pump, of which there are many varieties, those of Ludwig, Alvergniat, Geissler and Sprengel being the chief. The principle of action in all is the same. Ludwig's pump, which may be taken as a type, is represented in fig. 337. It consists of two fixed glass globes, *C* and *F*, the upper one communicating by means of the stopcock, *D*, and a stout indiarubber tube with another glass globe, *L*, which can be raised or lowered by means of a pulley; it also communicates by means of a stopcock, *B*, and a bent glass tube, *A*, with a gas receiver (not represented in the figure); *A* dips into a bowl of mercury, so that the gas may be received over mercury. The lower globe, *F*, communicates with *C* by means of the stopcock, *E*, with *I*, in which the blood is contained by the stopcock, *G*, and with a movable glass globe, *M*, similar to *L*, by means of the stopcock, *H*, and the stout indiarubber tube, *K*.

In order to work the pump, *L* and *M* are filled with mercury, the blood from which the gases are to be extracted is placed in the bulb *I*, the stopcocks, *H*, *E*, *D*, and *B*, being open, and *G* closed. *M* is raised by means of the pulley until *F* is full of mercury, and the air is driven out; *E* is then closed, and *L* is raised so that *C* becomes full of mercury, and the air is driven off. *B* is then closed. On lowering *L* the mercury runs into it from *C*, and a vacuum is established in *C*. On opening *E* and lowering *M*, a vacuum is similarly established in *F*; if *G* is now opened, the blood in *I* will enter into ebullition, and the gases will pass off into *F* and *C*, and on raising *M* and then *L*, the stopcock *B* being opened and *G* closed, the gas is driven through *A*, and is received into the receiver over mercury. By repeating this operation several times the whole of the gases of the specimen of blood is obtained, and may be estimated.

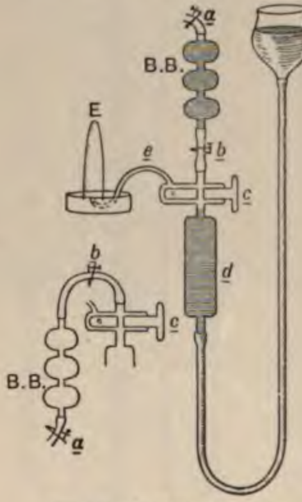


FIG. 338.—L. Hill's Air-pump.

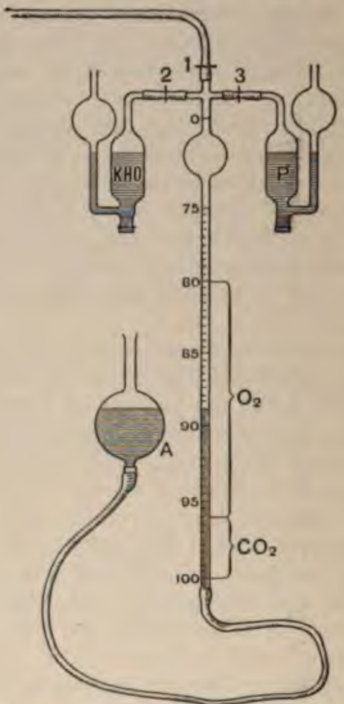


FIG. 339.—Waller's apparatus for gas analysis.

The very simple air-pump (fig. 338) devised by Leonard Hill will be, however, amply sufficient for most purposes. It consists of three glass bulbs; (B.B.), which we will call the *blood bulb*; this is closed above by a piece of tubing and a clip, *a*; this is connected by good indiarubber tubing to another bulb, *d*. Above *d*, however, there is a stopcock with two ways cut through it; one by means of which B.B. and *d* may be connected, as in the figure; and another seen in section, which unites *d* to the tube *e*, when the stopcock is turned through a right angle. In intermediate positions, the stopcock cuts off all communication from *d* to all parts of the apparatus above it; *d* is connected by tubing to a receiver, R, which can be raised or lowered at will. At first the whole apparatus is filled with mercury, R being raised. Then, *a* being closed, R is lowered, and when it is more than the height of the barometer (30 inches) below the top of B.B. the mercury falls and leaves the blood bulb empty; by lowering R still further, *d* can also be rendered a vacuum. A few drops of mercury should be left behind in B.B. B.B. is then detached from the rest of the apparatus and weighed, the clips, *a* and *b*, being tightly closed. Blood is then introduced into it by connecting the tube with the clip *a* on it to a cannula filled with blood inserted in an artery or vein of a living animal. Enough blood is withdrawn to fill about half of one of the bulbs. This is defibrinated by shaking it with the few drops of mercury left in the bulbs. It is then weighed again; the increase of weight gives the amount of blood which is being investigated. B.B. is then once more attached to the rest of the apparatus, hanging downwards, as in the side drawing in fig. 338, and the blood gases boiled off; these pass into *d*, which has been made a vacuum; and then by raising R again, the mercury rises in *d*, pushing the gases in front of it, through the tube, *e* (the stopcock being turned in the proper direction), into the eudiometer, E, which has been filled with and placed over mercury. The gas can then be measured and analysed.

Gas analysis.—There are many pieces of apparatus devised for this purpose. In physiology, however, we have generally to deal with only three gases, oxygen, nitrogen, and carbonic acid.

Waller's modification of Zuntz's more complete apparatus will be found very useful in performing gas analysis, say, of the expired air, or of the blood gases. A 100 c.c. measuring-tube graduated in tenths of a cubic centimetre between 75 and 100; a filling bulb (A) and two gas pipettes are connected up as in the diagram (fig. 339).

It is first charged with acidulated water up to the zero mark by raising the filling bulb, tap 1 being open. It is then filled with 100 c.c. of expired air, the filling bulb being lowered till the fluid in the tube has fallen to the 100 mark. Tap 1 is now closed. The amount of carbonic acid in the expired air is next ascertained; tap 2 is opened, and the air is expelled into the gas pipette containing strong caustic potash solution by raising the filling bulb until the fluid has risen to the zero mark of the measuring tube. Tap 2 is closed, and the air left in the gas pipette for a few minutes, during which the carbonic acid is absorbed by the potash. Tap 2 is then opened and the air drawn back into the measuring tube by lowering the filling bulb. The volume of air (*minus* the carbonic acid) is read, the filling bulb being adjusted so that its contents are at the same level as the fluid in the measuring tube. The amount of oxygen is next ascertained in a precisely similar manner by sending the air into the other gas pipette, which contains sticks of phosphorus in water, and measuring the loss of volume (due to absorption of oxygen) in the air when drawn back into the tube.

CHAPTER XXV

THE CHEMICAL COMPOSITION OF THE BODY

THE body is built up of a large number of chemical elements, which are in most instances united together into compounds.

The **elements** found in the body are carbon, nitrogen, hydrogen, oxygen, sulphur, phosphorus, fluorine, chlorine, iodine, silicon, sodium, potassium, calcium, magnesium, lithium, iron, and occasionally traces of manganese, copper, and lead.

Of these very few occur in the free state. Oxygen (to a small extent) and nitrogen are found dissolved in the blood; hydrogen is formed by putrefaction in the alimentary canal. With some few exceptions such as these, the elements enumerated above are found combined with one another to form what are called *compounds.*

The **compounds**, or, as they are generally termed in physiology, the *proximate principles*, found in the body are divided into—

(1) Mineral or inorganic compounds.

(2) Organic compounds, or compounds of carbon.

The **inorganic compounds** present are water, various acids (such as hydrochloric acid in the gastric juice), ammonia (as in the urine), and numerous salts, such as calcium phosphate in bone, sodium chloride in blood and urine, and many others.

The **organic compounds** are more numerous; they may be subdivided into—

Nitrogenous .	*Proteids—e.g.* albumin, myosin, casein. *Albuminoids—e.g.* gelatin, elastin. *Simpler nitrogenous bodies—e.g.* lecithin, creatine.
Non-nitrogenous	*Fats—e.g.* butter, fats of adipose tissue. *Carbohydrates—e.g.* sugar, starch. *Simple organic bodies—e.g.* cholesterin, lactic acids.

The subdivision of organic proximate principles into proteids, fats, and carbohydrates forms the starting-point of chemical physiology.

Carbohydrates.

The **Carbohydrates** are found chiefly in vegetable tissues, and many of them form important foods. Some carbohydrates are, however, found in or formed by the animal organism. The most important of these are *glycogen*, or animal starch; *dextrose*; and *lactose*, or milk sugar.

The carbohydrates may be conveniently defined as compounds of carbon, hydrogen, and oxygen, the two last named elements being in the proportion in which they occur in water. But this definition is only a rough one, and if pushed too far would include many substances like acetic acid, lactic acid, and inosite, which are not carbohydrates. Research has shown that the chemical constitution of the simplest carbohydrates is that of an aldehyde, or a ketone, and that the more complex carbohydrates are condensation products of the simple ones. In order, therefore, that we may understand the constitution of these substances, it is first necessary that we should understand what is meant by the terms aldehyde and ketone.

A primary alcohol is one in which the hydroxyl (OH) is attached to the last carbon atom of the chain; its end group is CH_2OH. Thus the formula for common alcohol (primary ethyl alcohol) is

$$CH_3.CH_2OH.$$

The formula for the next alcohol of the same series (primary propyl alcohol) is

$$CH_3.CH_2.CH_2OH.$$

If a primary alcohol is oxidised, the first oxidation product is called an *aldehyde*; thus ethyl alcohol yields acetic aldehyde:—

$$\underset{\text{[Ethyl alcohol.]}}{CH_3.CH_2OH} + O = \underset{\text{[Acetic aldehyde.]}}{CH_3.CHO} + H_2O.$$

The typical end-group CHO of the aldehyde is not stable, but is easily oxidisable to form the group COOH, and the compound so formed is called an acid; in this way acetic aldehyde forms acetic acid:—

$$\underset{\text{[Acetic aldehyde.]}}{CH_3.CHO} + O = \underset{\text{[Acetic acid.]}}{CH_3.COOH}.$$

The majority of the simple sugars are aldehydes of more complex alcohols than this; they are spoken of as *aldoses*. The readiness with which aldehydes are oxidisable renders them powerful reducing agents, and this furnishes us with some of the tests for the sugars.

Let us now turn to the case of the ketones. A secondary alcohol is one in which the OH group is attached to a central carbon atom; thus secondary propyl alcohol has the formula

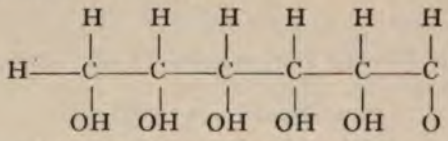
$$CH_3.CHOH.CH_3.$$

Its typical group is therefore CHOH. When this is oxidised, the first oxidation product is called a ketone, thus:—

$$\underset{\text{[Secondary propyl alcohol.]}}{CH_3.CHOH.CH_3} + O = \underset{\text{[Propyl ketone.]}}{CH_3.CO.CH_3} + H_2O.$$

It therefore contains the group CO in the middle of the chain. Some of the sugars are ketones of more complex alcohols; these are called *ketoses.* The only one of these which is of physiological interest is levulose.

The alcohols of which we have already spoken are called *monatomic,* because they contain only one OH group. Those which contain two OH groups (like glycol) are called diatomic; those which contain three OH groups (like glycerin) are called triatomic; and so on. The hexatomic alcohols are those which contain six OH groups. Three of these hexatomic alcohols with the formula $C_6H_8\,(OH)_6$ are of physiological interest; they are isomerides, and their names are sorbite, mannite, and dulcite. By careful oxidation their aldehydes and ketones can be obtained; these are the simple sugars; thus, dextrose is the aldehyde of sorbite; mannose is the aldehyde of mannite; levulose is the ketone of mannite; and galactose is the aldehyde of dulcite. These sugars all have the empirical formula $C_6H_{12}O_6$. The constitutional formula for dextrose is:—



$$\begin{array}{ccccccccccccc} & & H & & H & & H & & H & & H & & H \\ & & | & & | & & | & & | & & | & & | \\ H & — & C & — & C & — & C & — & C & — & C & — & C \\ & & | & & | & & | & & | & & | & & | \\ & & OH & & OH & & OH & & OH & & OH & & O \end{array}$$

By further oxidation, the sugars yield acids with various names. If we take such a sugar as a typical specimen, we see that their general formula is

$$C_nH_{2m}O_m$$

and as a general rule $n = m$; that is, the number of oxygen and carbon atoms are equal. This number in the case of the sugars already mentioned is six. Hence they are called *hexoses.*

Sugars are known to chemists, in which this number is 3, 4, 5, 7, etc., and these are called trioses, tetroses, pentoses, heptoses, etc. The majority of these have no physiological interest. It should, however, be mentioned that a pentose has been obtained from the nucleoproteid of the pancreas, of the liver, and of yeast. If the pentoses that are found in various plants are given to an animal, they are excreted in great measure unchanged in the urine.

The hexoses are of great physiological importance. The principal ones are dextrose, levulose, and galactose. These are called *monosaccharides.* Another important group of sugars are called *disaccharides;* these are formed by what is called condensation; that is, two molecules of monosaccharide combine together with the loss of a molecule of water, thus:—

$$C_6H_{12}O_6 + C_6H_{12}O_6 = C_{12}H_{22}O_{11} + H_2O.$$

The principal members of the disaccharide group are cane-sugar, lactose, and maltose. If more than two molecules of the monosaccharide group undergo a corresponding condensation, we get what are called *polysaccharides*.

$$nC_6H_{12}O_6 = (C_6H_{10}O_5)_n + nH_2O.$$

The polysaccharides are starch, glycogen, various dextrins, cellulose, and gums. We may, therefore, arrange the important carbohydrates of the hexose family in a tabular form as follows:—

1. Monosaccharides or Glucoses, $C_6H_{12}O_6$.	2. Disaccharides, Sucroses, or Saccharoses, $C_{12}H_{22}O_{11}$.	3. Polysaccharides or Amyloses $(C_6H_{10}O_5)_n$.
+ **Dextrose.** − **Levulose.** + **Galactose.**	+ **Cane sugar.** + **Lactose.** + **Maltose.**	+ **Starch.** + **Glycogen.** + **Dextrin.** **Cellulose.** **Gums.**

The + and − signs in the above list indicate that the substances to which they are prefixed are dextro- and levo-rotatory respectively as regards polarised light. (See Polarimeter, p. 404.) The formulæ given above are merely empirical; the quantity n in the starch group is variable and often large. The following are the chief facts in relation to each of the principal carbohydrates.

Dextrose or Grape Sugar.—This carbohydrate is found in fruits, honey, and in minute quantities in the blood and numerous tissues, organs, and fluids of the body. It is the form of sugar found in large quantities in the blood and urine in the disease known as *diabetes*.

Dextrose is soluble in hot and cold water and in alcohol. It is crystalline, but not so sweet as cane sugar. When heated with strong potash certain complex acids are formed which have a yellow or brown colour. This constitutes *Moore's test* for sugar. In alkaline solutions dextrose reduces salts of silver, bismuth, mercury, and copper. The reduction of cupric to cuprous salts constitutes *Trommer's test*, which is performed as follows: put a few drops of copper sulphate into a test-tube, then solution of dextrose, and then strong caustic potash. On adding the potash a precipitate is first formed which dissolves, forming a blue solution. On boiling this a yellow or red precipitate (cuprous hydrate or oxide) forms.

On boiling a solution of dextrose with an alkaline solution of picric acid, a dark red opaque solution due to reduction to picramic acid is produced.

Another important property of grape sugar is that under the influence of yeast it is converted into alcohol and carbonic acid ($C_6H_{12}O_6 = 2C_2H_6O + 2CO_2$).

Dextrose may be estimated by the fermentation test, by the polarimeter, and by the use of Fehling's solution. The last method is the most important: it rests on the same principles as Trommer's test, and we shall study it in connection with diabetic urine.

Levulose.—When cane sugar is treated with dilute mineral acids it undergoes a process known as *inversion*—*i.e.*, it takes up water and is converted into equal parts of dextrose and levulose. The previously dextro-rotatory solution of cane sugar then becomes levo-rotatory, the levo-rotatory power of the levulose being greater than the dextro-rotatory power of the dextrose formed. Hence the term *inversion*. The same hydrolytic change is produced by certain ferments, such as the invert ferment of the intestinal juice.

Pure levulose can be crystallised, but so great is the difficulty of obtaining crystals of it that one of its names was *uncrystallisable sugar*. Small quantities of levulose have been found in blood, urine, and muscle. It has been recommended as an article of diet in diabetes in place of ordinary sugar; in this disease it does not appear to have the harmful effect that other sugars produce. Levulose gives the same general reactions as dextrose.

Galactose is formed by the action of dilute mineral acids or inverting ferments on lactose. It resembles dextrose in its action on polarised light, in reducing cupric salts in Trommer's test, and in being directly fermentable with yeast. When oxidised by means of nitric acid it yields an acid called *mucic acid* ($C_6H_{10}O_8$), which is only slightly soluble in water. Dextrose when treated in this way yields an isomeric acid—*i.e.*, an acid with the same empirical formula, called *saccharic acid*, which is very soluble in water.

Cane Sugar is generally distributed in the vegetable kingdom, but especially in the juices of the sugar cane, beetroot, mallow, and sugar maple. It is a substance of great importance as a food. It undergoes inversion in the alimentary canal. It is crystalline, and dextro-rotatory. With Trommer's test it gives a blue solution, but no reduction occurs in boiling. After inversion it is, of course, strongly reducing.

Inversion may be accomplished by boiling with dilute mineral acids, or by means of inverting ferments such as that occurring in the intestinal juice. It then takes up water, and is split into equal parts of dextrose and levulose.

$$\underset{\text{[Cane sugar.]}}{C_{12}H_{22}O_{11}} + H_2O = \underset{\text{[Dextrose.]}}{C_6H_{12}O_6} + \underset{\text{[Levulose.]}}{C_6H_{12}O_6}.$$

With yeast, cane sugar is first inverted by means of a special soluble ferment secreted by the yeast cells, and then there is an alcoholic fermentation of the glucoses so formed.

Lactose, or Milk Sugar, occurs in milk. It is occasionally found in the urine of women in the early days of lactation, or after weaning. It is crystallisable, dextro-rotatory, much less soluble in water than other sugars, and has only a slightly sweet taste. It gives Trommer's test, but when the reducing power is tested quantitatively by Fehling's solution it is found to be a less powerful reducing agent than dextrose, in the proportion of 7 to 10.

When hydrolysed by similar agencies as those mentioned in connection with cane sugar, it takes up water and splits into dextrose and galactose.

$$\underset{\text{[Lactose.]}}{C_{12}H_{22}O_{11}} + H_2O = \underset{\text{[Dextrose.]}}{C_6H_{12}O_6} + \underset{\text{[Galactose.]}}{C_6H_{12}O_6}.$$

With yeast it is first inverted, and then alcohol is formed. This, however, occurs slowly.

The lactic acid fermentation which occurs when milk turns sour is brought about by lactic acid micro-organisms which are somewhat similar to yeast cells. Putrefactive bacteria in the intestine bring about the same result. The two stages of the lactic acid fermentation are represented in the following equations:—

$$(1.)\ \underset{\text{[Lactose.]}}{C_{12}H_{22}O_{11}} + H_2O = \underset{\text{[Lactic acid.]}}{4C_3H_6O_3}.$$

$$(2.)\ \underset{\text{[Lactic acid.]}}{4C_3H_6O_3} = \underset{\text{[Butyric acid.]}}{2C_4H_8O_2} + 4CO_2 + 4H_2.$$

Maltose is the chief end product of the action of malt diastase on starch, and is also formed as an intermediate product in the action of dilute sulphuric acid on the same substance. It is the chief sugar formed from starch by the diastatic ferments contained in the saliva and pancreatic juice. It can be obtained in the form of acicular crystals, and is strongly dextro-rotatory. It gives Trommer's test; but its reducing power, as measured by Fehling's solution, is one-third less than that of dextrose. With yeast it yields alcohol.

By prolonged boiling with water, or, more readily, by boiling with a dilute mineral acid, or by means of an inverting ferment, such as occurs in the intestinal juice, it is converted into dextrose.

$$\underset{\text{[Maltose.]}}{C_{12}H_{22}O_{11}} + H_2O = \underset{\text{[Dextrose.]}}{2C_6H_{12}O_6}.$$

Phenyl Hydrazine Test.—The three important reducing sugars with which we have to deal in physiology are dextrose, lactose, and maltose. They may be distinguished by their relative reducing powers on Fehling's solution, or by the characters of their osazones. The osazone is formed in each case by adding phenyl hydrazine hydrochloride, and sodium acetate, and boiling the mixture for half an hour. In each case the osazone is deposited in the form of bright canary-coloured, needle-like crystals, usually in bunches, which differ in their crystalline form, melting-point, and solubilities. Cane sugar does not yield an osazone.

Starch is widely diffused through the vegetable kingdom. It occurs in nature in the form of microscopic grains, varying in size and appearance, according to their source. Each consists of a central spot, round which more or less concentric envelopes of starch proper or granulose alternate with layers of cellulose. Cellulose has very little digestive value, but starch is a most important food.

Starch is insoluble in cold water: it forms an opalescent solution in boiling water, which if concentrated gelatinises on cooling. Its most characteristic reaction is the blue colour it gives with iodine.

On heating starch with mineral acids, dextrose is formed. By the action of diastatic ferments, maltose is the chief end product. In both cases dextrin is an intermediate stage in the process.

Before the formation of dextrin the starch solution loses its opalescence, a substance called *soluble starch* being formed. This, like native starch, gives a blue colour with iodine. Although the molecular weight of starch is unknown, the formula for soluble starch is probably $5(C_{12}H_{20}O_{10})_{20}$. Equations that represent the formation of sugars and dextrins from this are very complex, and are at present only hypothetical.

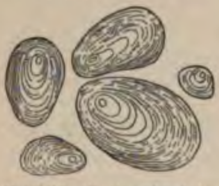


FIG. 340.—Grains of potato starch.

Dextrin is the name given to the intermediate products in the hydration of starch or glycogen, and two chief varieties are distinguished :—*erythro-dextrin*, which gives a reddish-brown colour with iodine; and *achroo-dextrin*, which does not.

It is readily soluble in water, but insoluble in alcohol and ether. It is gummy and amorphous. It does not give Trommer's test, nor does it ferment with yeast. It is dextro-rotatory. By hydrating agencies it is converted into glucose.

Glycogen, or animal starch, is found in liver, muscle, and white blood corpuscles. It is also abundant in all embryonic tissues.

Glycogen is a white tasteless powder, soluble in water, but it forms, like starch, an opalescent solution. It is insoluble in alcohol and ether. It is dextro-rotatory. With Trommer's test it gives a blue solution, but no reduction occurs on boiling.

With iodine it gives a reddish or port-wine colour, very similar to that given by erythro-dextrin. Dextrin may be distinguished from glycogen by (1) the fact that it gives a clear, not an opalescent, solution with water; and (2) it is not precipitated by basic lead acetate as glycogen is. It is, however, precipitated by basic lead acetate and ammonia. (3) Glycogen is precipitated by 55 per cent. of alcohol; the dextrins require 85 per cent. or more.

Cellulose.—This is the colourless material of which the cell-walls and woody fibres of plants are composed. By treatment with strong mineral acids it is, like starch, converted into glucose, but with much greater difficulty. The various digestive ferments have little or no action on cellulose; hence the necessity of boiling starch before it is taken as food. Boiling bursts the cellulose envelopes of the starch grains, and so allows the digestive juices to get at the starch proper.

Cellulose is found in a few animals, as in the test or outer investment of the Tunicates.

[**Inosite**, or muscle sugar ($C_6H_{12}O_6$), is found in muscle, kidney, liver, and other parts of the body in small quantities. It is also largely found in the vegetable kingdom. It is crystallisable, and has the same formula as the glucoses. It is, however, not a sugar, and careful analysis has shown that it really belongs to the aromatic series.]

The Fats.

Fat is found in small quantities in many animal tissues. It is, however, found in large quantities in three situations, viz., marrow, adipose tissue, and milk.

The contents of the fat cells of adipose tissue are fluid during life, the normal temperature of the body (37° C., or 99° F.) being considerably above the melting-point (25° C.) of the mixture of the fats found there. These fats are three in number, and are called *palmitin*, *stearin*, and *olein*. They differ from one another in chemical composition and in certain physical characters, such as melting-point and solubilities. Olein melts at $-5°$ C., palmitin at 45° C., and stearin at 53-66° C. It is thus olein which holds the other two dissolved at the body temperature. Fats are all soluble in hot alcohol, ether, and chloroform, but insoluble in water.

Chemical Constitution of the Fats.—The fats are compounds of fatty acids with glycerin, and may be termed *glycerides* or *glyceric ethers*. The term *hydrocarbon*, applied to them by some authors, is wholly incorrect.

The fatty acids form a series of acids derived from the monatomic alcohols by oxidation. Thus, to take ordinary ethyl alcohol, C_2H_6O, the first stage in oxidation is the removal of two atoms of hydrogen to form aldehyde, C_2H_4O; on further oxidation an atom of oxygen is added to form acetic acid, $C_2H_4O_2$.

A similar acid can be obtained from all the other alcohols, thus:—

From	methyl	alcohol	$CH_3.HO$,	formic	acid	$H.COOH$	is obtained.
,,	ethyl	,,	$C_2H_5.HO$,	acetic	,,	$CH_3.COOH$	,,
,,	propyl	,,	$C_3H_7.HO$,	propionic	,,	$C_2H_5.COOH$	,,
,,	butyl	,,	$C_4H_9.HO$,	butyric	,,	$C_3H_7.COOH$	,,
,,	amyl	,,	$C_5H_{11}.HO$,	valeric	,,	$C_4H_9.COOH$	,,
,,	hexyl	,,	$C_6H_{13}.HO$,	caproic	,,	$C_5H_{11}.COOH$	,,

and so on,

Or in general terms:—

From the alcohol with formula $C_nH_{2n+1}.HO$, the acid with formula $C_{n-1}H_{2n-1}.COOH$ is obtained. The sixteenth term of this series has the formula $C_{15}H_{31}.COOH$, and is called **palmitic acid**; the eighteenth has the formula $C_{17}H_{35}.COOH$, and is called **stearic acid**. Each acid, as will be seen, consists of a radicle, $C_{n-1}H_{2n-1}CO$, united to hydroxyl (OH). **Oleic acid**, however, is not a member of this series, but belongs to a somewhat similar series known as the *acrylic series*, of which the general formula is $C_{n-1}H_{2n-3}.COOH$. It is the eighteenth term of the series, and its formula is $C_{17}H_{33}.COOH$.

The first member of the group of alcohols from which this acrylic series of acids is obtained is called *allyl alcohol* ($CH_2:CH.CH_2OH$); the aldehyde of this is *acrolein* ($CH_2:CH.CHO$), and the formula for the acid (acrylic acid) is $CH_2:CH.COOH$. It will be noticed that two of the carbon atoms are united by two valencies, and these bodies are therefore unsaturated; they are unstable and are prone to undergo by uniting with another element a conversion into bodies in which the carbon atoms are united by only one bond. This accounts for their reducing action, and it is owing to this that the colour reactions with osmic acid and Sudan III. are due. Fat which contains any member of the acrylic series like oleic acid blackens osmic acid, by reducing it to a lower (black) oxide. Fats like palmitin and stearin do not give this reaction.

Glycerin or **Glycerol** is a triatomic alcohol, $C_3H_5(HO)_3$—*i.e.*, three atoms of hydroxyl united to a radicle glyceryl (C_3H_5). The hydrogen in the hydroxyl atoms is replaceable by other organic radicles. As an example, take the radicle of acetic acid called *acetyl* ($CH_3.CO$). The following formulæ represent the derivatives that can be obtained by replacing one, two, or all three hydroxyl hydrogen atoms in this way:—

$$C_3H_5\left\{\begin{array}{l}OH\\OH\\OH\end{array}\right. \quad C_3H_5\left\{\begin{array}{l}OH\\OH\\O.CH_3.CO\end{array}\right. \quad C_3H_5\left\{\begin{array}{l}OH\\O.CH_3.CO\\O.CH_3.CO\end{array}\right. \quad C_3H_5\left\{\begin{array}{l}O.CH_3.CO\\O.CH_3.CO\\O.CH_3.CO\end{array}\right.$$

[Glycerin.] [Monoacetin.] [Diacetin.] [Triacetin.]

Triacetin is a type of a neutral fat; stearin, palmitin, and olein ought more properly to be called *tristearin*, *tripalmitin*, and *triolein* respectively. Each consists of glycerin in which the three atoms of hydrogen in the hydroxyls are replaced by radicles of the fatty acid. This is represented in the following formulæ:—

	Acid.		*Radicle.*		*Fat.*
Palmitic acid	$C_{15}H_{31}.COOH$	Palmityl	$C_{15}H_{31}.CO$	Palmitin	$C_3H_5(OC_{15}H_{31}.CO)_3$
Stearic acid	$C_{17}H_{35}.COOH$	Stearyl	$C_{17}H_{35}.CO$	Stearin	$C_3H_5(OC_{17}H_{35}.CO)_3$
Oleic acid	$C_{17}H_{33}.COOH$	Oleyl	$C_{17}H_{33}.CO$	Olein	$C_3H_5(OC_{17}H_{33}.CO)_3$

Decomposition Products of the Fats.—The fats split up into the substances out of which they are built up.

Under the influence of superheated steam, mineral acids, and in the body by means of certain ferments (for instance, the fat-splitting ferment, steapsin, of the pancreatic juice), a fat combines with water and splits into glycerin and the fatty acid. The following equation represents what occurs in a fat, taking tripalmitin as an example:—

$$\underset{\text{[Tripalmitin—a fat.]}}{C_3H_5(O.C_{15}H_{31}CO)_3} + 3H_2O = \underset{\text{[Glycerin.]}}{C_3H_5(OH)_3}\ \underset{\text{[Palmitic acid—a fatty acid.}}{3C_{15}H_{31}CO.OH.}$$

In the process of **saponification** much the same sort of reaction occurs, the final products being glycerin and a compound of the base with the fatty acid which is called a *soap*. Suppose, for instance, that potassium hydrate is used; we get—

$$\underset{\text{[Tripalmitin—a fat.]}}{C_3H_5(O.C_{15}H_{31}CO)_3} + 3KHO = \underset{\text{[Glycerin.]}}{C_3H_5(OH)_3} + \underset{\text{[Potassium palmitate—a soap.]}}{3C_{15}H_{31}CO.OK.}$$

Emulsification.—Another change that fats undergo in the body is very different from saponification. It is a physical rather than a chemical change; the fat is broken up into very small globules, such as are seen in the natural *emulsion*—milk.

Lecithin ($C_{42}H_{84}NPO_9$).—This is a very complex fat, which yields on decomposition not only glycerin and fatty acids (*stearic* and *oleic*), but phosphoric acid, and an alkaloid [$N.(CH_3)_3C_2H_6O_2$] called *choline* in addition. This substance is found to a great extent in the nervous system (see p. 175), and to a small extent in bile. Together with **cholesterin**, a crystallisable, monatomic alcohol ($C_{27}H_{45}.HO$), which we shall consider more at length in connection with the bile, it is found in small quantities in the protoplasm of all cells.

The Proteids.

The **proteids** are the most important substances that occur in animal and vegetable organisms; none of the phenomena of life occur without their presence; and though it is impossible to state positively that they occur as such in living protoplasm, they are invariably obtained by subjecting living structures to analysis.

Proteids are highly complex compounds of carbon, hydrogen, oxygen, nitrogen, and sulphur occurring in a solid viscous condition or in solution in nearly all the liquids and solids of the body. The different members of the group present differences in chemical and physical properties. They all possess, however, certain common chemical reactions, and are united by a close genetic relationship.

The various proteids differ a good deal in elementary composition. Hoppe-Seyler gives the following percentages:—

	C	H	N	S	O
From	51·5	6·9	15·2	0·3	20·9
To	54·5	7·3	17·0	2·0	23·5

We are, however, not acquainted with the constitutional formula of proteid substances. There have been many theories on the subject, but practically all that is known with certainty is that many different substances may be obtained by the decomposition of proteids. How they are built up into the proteid molecule is unknown. The decompositions that occur in the body are, moreover, different from those which can be made to occur in the laboratory; hence the conclusion that living protoplasm differs from the non-living proteid material obtainable from it.

(1) In the body. Carbonic acid, water, and urea are the chief final products. Glycocine, leucine, creatine, uric acid, ammonia, etc., are probably intermediate products. Carbohydrates (glycogen) and fats may also originate from proteids.

(2) Outside the body. Various strong reagents break up proteids into ammonia, carbonic acid, amines, hexone bases, fatty acids, amido-acids like leucine and arginine, and aromatic compounds like tyrosine.

Solubilities.—All proteids are insoluble in alcohol and ether. Some are soluble in water, others insoluble. Many of the latter are soluble in weak saline solutions. Some are insoluble, others soluble in concentrated saline solutions. It is on these varying solubilities that proteids are classified.

All proteids are soluble with the aid of heat in concentrated mineral acids and alkalies. Such treatment, however, decomposes as well as dissolves the proteid. Proteids are also soluble in gastric and pancreatic juices; but here, again, they undergo a change, being converted into a hydrated variety of proteid, of smaller molecular weight, called *peptone.* The intermediate substances formed in this process are called *proteoses* or *albumoses.* Commercial peptone contains a mixture of proteoses and true peptone.

Heat Coagulation.—Most native proteids, like white of egg, are rendered insoluble when their solutions are heated. The temperature of heat coagulation differs in different proteids; thus myosinogen and fibrinogen coagulate at 56° C., serum albumin and serum globulin at about 75° C.

The proteids which are coagulated by heat come under two classes: the *albumins* and the *globulins.* These differ in solubility; the albumins are soluble in distilled water, the globulins require salts to hold them in solution.

Indiffusibility.—The proteids (peptones excepted) belong to the class of substances called *colloids* by Thomas Graham; that is, they pass with difficulty, or not at all, through animal membranes. In the construction of dialysers, vegetable parchment is largely used.

Proteids may thus be separated from diffusible (*crystalloid*) substances like salts, but the process is a tedious one. If some serum or white of egg is placed in a dialyser (fig. 341) and distilled water outside, the greater amount of the salts passes into the water through the membrane and is replaced by water; the two proteids albumin and globulin remain inside; the globulin is, however, precipitated, as the salts which previously kept it in solution are removed.

Crystallisation.—Hæmoglobin, the red pigment of the blood, is a proteid substance and is crystallisable (for further details, see The Blood, Chapter XXVI.). Like other proteids it has an enormously large molecule; though crystalline, it is not, however, crystalloid in Graham's sense of that term. Blood pigment is not the only crystallisable proteid. Long ago crystals of proteid (globulin or vitellin) were observed in the aleurone grains of many seeds, and in the somewhat similar granules occurring in the egg-yolk of some fishes and amphibians. By appropriate methods these have been separated and re-crystallised. Further, egg-albumin itself has been crystallised. If a solution of white of egg is diluted with an equal volume of saturated solution of ammonium sulphate, the globulin present is precipitated and is removed by filtration. The filtrate is now allowed to remain some days at the temperature of the air, and as it becomes more concentrated from evaporation, minute spheroidal globules and finally minute needles, either aggregated or separate, make their appearance (Hofmeister). Crystallisation is more rapid if a little acetic or sulphuric acid is added (Hopkins). Serum albumin (from horse and rabbit) has also been similarly crystallised (Gürber).

Action on Polarised Light.—All proteids are levo-rotatory, the amount of rotation varying with individual proteids. Several of the compound proteids, *e.g.*, hæmoglobin, and nucleo-proteids are dextro-rotatory, though their proteid components are levo-rotatory (Gamgee).

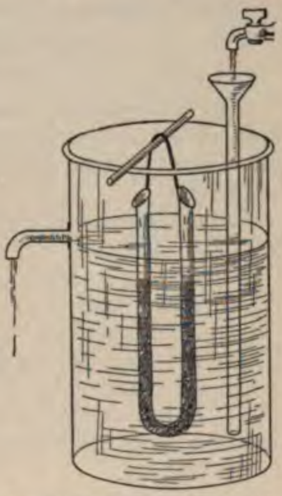


FIG. 341.—Dialyser made of a tube of parchment paper, suspended in a vessel through which water is kept flowing.

Colour Reactions.—The principal colour reactions by which proteids are recognised are the following:—

(1) The *xantho-proteic reaction;* if a few drops of nitric acid are added to a solution of a proteid like white of egg, the result is a white precipitate; this and the surrounding liquid become yellow on boiling and are turned orange by ammonia. The preliminary white precipitate is not given by some proteids like peptones; but the colours are the same.

(2) *Millon's reaction.* Millon's reagent is a mixture of mercuric and mercurous nitrate with excess of nitric acid. This gives a white

precipitate with proteids which is turned brick-red on boiling. This reaction and the preceding (xanthroproteic) depend on the presence in proteids of aromatic radicles.

(3) *Copper sulphate* (*Rose's or Piotrowski's*) *test.* A trace of copper sulphate and excess of strong caustic potash give with most proteids a violet solution. Proteoses and peptones, however, give a rose-red colour instead; this same colour is given by the substance called *biuret;* hence the test is generally called the *biuret reaction.* This name does not imply that biuret is present in proteid; but both proteid and biuret give the reaction because they possess a common radicle, probably CONH.

Biuret is formed by heating solid urea; ammonia passes off and leaves biuret thus :—

$$\underset{\text{[Urea.]}}{2CON_2H_4} - \underset{\text{[Ammonia.]}}{NH_3} = \underset{\text{[Biuret.]}}{C_2O_2N_3H_5}.$$

(4) *Adamkiewicz reaction* (Hopkins' modification). When a solution of proteid is added to a dilute solution of glyoxylic acid, and then excess of sulphuric acid is added, an intense violet colour is obtained.

Precipitants of Proteids.—Solutions of most proteids are precipitated by:—

1. Strong acids like nitric acid.
2. Picric acid.
3. Acetic acid and potassium ferrocyanide.
4. Acetic acid and excess of a neutral salt like sodium sulphate; when these are boiled with the proteid solution.
5. Salts of the heavy metals like copper sulphate, mercuric chloride, lead acetate, silver nitrate, etc.
6. Tannin.
7. Alcohol.
8. Saturation with certain neutral salts such as ammonium sulphate.

It is necessary that the words *coagulation* and *precipitation* should in connection with proteids be carefully distinguished. The term *coagulation* is used when an insoluble proteid (coagulated proteid) is formed from a soluble one. This may occur:

1. When a proteid is heated—*heat coagulation;*
2. Under the influence of a ferment; for instance, when a curd is formed in milk by rennet or a clot in shed blood by the fibrin ferment —*ferment coagulation;*
3. When an insoluble precipitate is produced by the addition of certain reagents (nitric acid, picric acid, tannin, etc.).

There are, however, other precipitants of proteids in which the precipitate formed is readily soluble in suitable reagents like saline solutions, and the proteid continues to show its typical reactions.

Such precipitation is not coagulation. Such a precipitate is produced by saturation with ammonium sulphate. Certain proteids, called *globulins*, are more readily precipitated by such means than others. Thus, serum globulin is precipitated by half-saturation with ammonium sulphate. Full saturation with ammonium sulphate precipitates all proteids but peptone. The globulins are precipitated by certain salts, like sodium chloride and magnesium sulphate, which do not precipitate the albumins.

The precipitation produced by alcohol is peculiar in that after a time it becomes a coagulation. Proteid freshly precipitated by alcohol is readily soluble in water or saline media; but after it has been allowed to stand some weeks under alcohol it becomes more and more insoluble. Albumins and globulins are most readily rendered insoluble by this method; proteoses and peptones are never rendered insoluble by the action of alcohol. This fact is of value in the separation of these proteids from others.

Classification of Proteids.

Both animal and vegetable proteids can be divided into the following classes. We shall, however, be chiefly concerned with the animal proteids:—

If we use the term proteid in the widest sense, the first main subdivision of these substances is into—

A. The Simple Proteids.
B. The Conjugated or Compound Proteids.
C. The Albuminoids.
D. The Protamines.

We will take these classes one by one.

A. THE SIMPLE PROTEIDS.

Class I. **Albumins.**—These are soluble in water, in dilute saline solutions, and in saturated solutions of sodium chloride and magnesium sulphate. They are, however, precipitated by saturating their solutions with ammonium sulphate. Their solutions are coagulated by heat, usually at 70-73° C. Serum albumin, egg albumin, and lactalbumin are instances.

Class II. **Globulins.**—These are insoluble in water, soluble in dilute saline solutions, and insoluble in concentrated solutions of neutral salts like sodium chloride, magnesium sulphate, and ammonium sulphate. A globulin dissolved in a dilute saline solution may therefore be precipitated—

1. By removing the salt—by dialysis (see p. 396).
2. By increasing the amount of salt. The best salts to employ are

ammonium sulphate (half-saturation) or magnesium sulphate (complete saturation). This method is often called "salting out."

The globulins are coagulated by heat; the temperature of heat coagulation varies considerably. The following are instances:—

(*a*) Fibrinogen
(*b*) Serum globulin (paraglobulin) } in blood-plasma.
(*c*) Paramyosinogen in muscle.
(*d*) Crystallin in the crystalline lens.

If we compare together these two classes of proteids, the most important of the native proteids, we find that they all give the same general tests, that all are coagulated by heat, but that they differ in their solubilities. This difference in solubility may be stated in tabular form as follows:—

Reagent.	Albumin.	Globulin.
Water	soluble	insoluble
Dilute saline solution	soluble	soluble
Saturated solution of magnesium sulphate or sodium chloride . . .	soluble	insoluble
Half-saturated solution of ammonium sulphate	soluble	insoluble
Saturated solution of ammonium sulphate	insoluble	insoluble

Class III. **Proteoses**
Class IV. **Peptones** { These products of digestion will be studied in connection with that subject.

Class V. **Coagulated Proteids.**—There are two main subdivisions of these:—

(*a*) Proteids in which coagulation has been produced by heat; they are insoluble in water, saline solutions, weak acids, and weak alkalis; they are soluble after prolonged boiling in concentrated mineral acids; dissolved by gastric and pancreatic juices, they give rise to peptones.

(*b*) Proteids in which coagulation has been produced by ferments:—i. Fibrin (see Blood). ii. Myosin (see Muscle). iii. Casein (see Milk).

Appendix to the class of simple proteids. **Albuminates** are compounds of proteid with mineral substances. Thus, if a solution of copper sulphate is added to a solution of albumin a precipitate of copper albuminate is obtained. Similarly, by the addition of other salts of the heavy metals other metallic albuminates are obtainable.

The albuminates which are obtained by the action of dilute acids and alkalis on either albumins or globulins are, however, of greater physiological interest, and it is to these we shall confine our attention.

The general properties of the *acid-albumin* or *syntonin*, and the *alkali-albumin*, which are thereby respectively formed, are as follows: they are insoluble in pure water, but are soluble in either acid or alkali, and are precipitated by neutralisation unless certain salts, like sodium phosphate, are present. Like globulins, they are precipitated by saturation with such neutral salts as sodium chloride and magnesium sulphate. They are not coagulated by heat.

A variety of alkali-albumin (probably a compound containing a large quantity of alkali) may be formed by adding strong potash to undiluted white of egg. The resulting jelly is called *Lieberkühn's jelly*. A similar jelly is formed by adding strong acetic acid to undiluted egg-white.

The halogens (chlorine, bromine, and iodine) also form albuminates, and may be used for the precipitation of proteids.

B. The Conjugated Proteids.

These complex substances are compounds of albuminous substances with other organic materials, which are, as a rule, also of complex nature. They may be divided into the following groups:—

1. HÆMOGLOBIN and its allies. These are compounds of proteid with an iron-containing pigment. All will be fully discussed under Blood.

2. GLUCO-PROTEIDS. These are compounds of proteids with members of the carbohydrate group. This class includes the mucins and substances allied to mucins called mucoids.

Mucin.—This is a widely distributed substance, occurring in epithelial cells or shed out by them (mucus, mucous glands, goblet cells).

There are several varieties of mucin, but all agree in the following points:—

(*a*) Physical character. Viscid and tenacious.

(*b*) Precipitability from solutions by acetic acid. They are soluble in dilute alkalis, like lime water.

(*c*) They are all compounds of a proteid with a carbohydrate radicle, which by treatment with dilute mineral acid can be hydrated into a reducing but non-fermentable sugar.

It is probable that the carbohydrate radicle may differ in different mucins; in some cases it is certainly the case that the so-called sugar derived from it is not sugar, but a nitrogenous derivative of sugar called glucosamine ($C_6H_{11}O_5NH_2$)—*i.e.*, glucose in which HO is replaced by NH_2.

The **mucoids** generally resemble the mucins but differ from them in minor details. The term is applied to the mucin-like substances found in the ground substance of connective tissues (tendo-mucoid, chondro-mucoid, etc.). Another (ovo-mucoid) is found in white of egg, and others (pseudo-mucin and paramucin) are occasionally found in dropsical effusions.

Dr Pavy has shown that a *small* quantity of a similar carbohydrate can be split off from various other proteids, which we have already classified as simple proteids.

3. NUCLEINS AND NUCLEO-PROTEIDS. These are compounds of proteid with a complex organic acid called nucleic acid, which contains phosphorus.

Nucleo-proteids.—Compounds of proteids with nuclein. They are found in the nuclei and protoplasm of cells. Caseinogen of milk and vitellin of egg-yolk are similar substances. In physical characters they often closely simulate mucin; in fact, the substance called mucin in the bile is in some animals a nucleo-proteid. They may be distinguished from mucin by the fact that they yield on gastric digestion not only peptone but also an insoluble residue of nuclein which is soluble in alkalis, is precipitable by acetic acid from such a solution, and contains a high percentage (10·11) of phosphorus.

Some of the nucleo-proteids also contain iron, and it is probable that the normal supply of iron to the body is contained in the nucleo-proteids, or hæmatogens (Bunge), of plant and animal cells.

The relationship of nucleo-proteids to the coagulation of the blood is described in the next chapter.

Nucleo-proteids may be prepared from cellular structures like testis, thymus, kidney, etc., by two methods:—

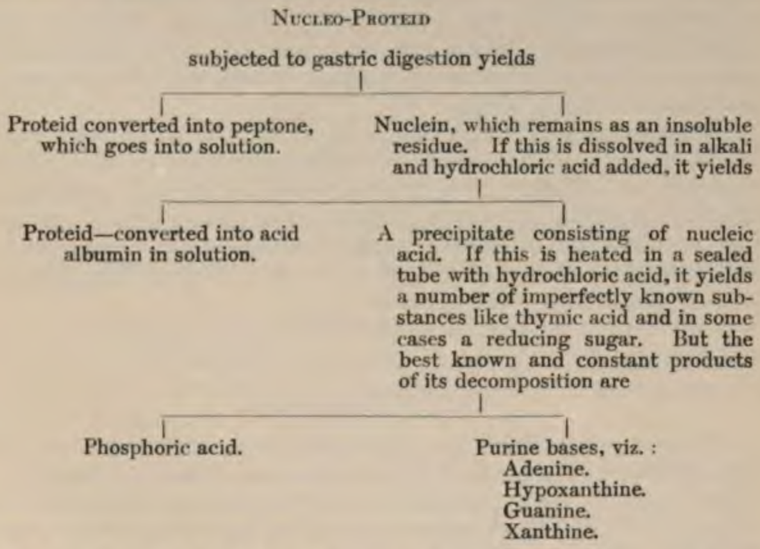
1. *Wooldridge's method.*—The organ is minced and soaked in water for twenty-four hours. Acetic acid added to the aqueous extract precipitates the nucleo-proteid, or, as Wooldridge called it, *tissue fibrinogen.*

2. *Sodium chloride method.*—The minced organ is ground up in a mortar with solid sodium chloride; the resulting viscous mass is poured into excess of distilled water, and the nucleo-proteid rises in strings to the top of the water.

The solvent usually employed for a nucleo-proteid, whichever method it is prepared by, is a 1 per cent. solution of sodium carbonate.

Nuclein is the chief constituent of cell-nuclei. Its physical characters are somewhat like those of mucin, but it differs chemically in its high percentage of phosphorus. It is identical with the chromatin of histologists (see p. 11). On decomposition, it yields an organic acid called *nucleic* acid, together with a variable amount of proteid. Nucleic acid on decomposition yields phosphoric acid and various bases of the xanthine group. Some forms of nuclein, called *pseudo-nuclein,* such as are obtained from casein and vitellin, differ from the true nucleins in not yielding these xanthine compounds, or, as they are sometimes termed, *alloxuric* or *purine* bases. The purine bases are closely allied chemically to uric acid, and we shall have to consider them again in relation to that substance.

The following diagrammatic way of representing the decomposition of nucleo-proteid will assist the student in remembering the relationships of these substances:—



NUCLEO-PROTEID

subjected to gastric digestion yields

Proteid converted into peptone, which goes into solution.

Nuclein, which remains as an insoluble residue. If this is dissolved in alkali and hydrochloric acid added, it yields

Proteid—converted into acid albumin in solution.

A precipitate consisting of nucleic acid. If this is heated in a sealed tube with hydrochloric acid, it yields a number of imperfectly known substances like thymic acid and in some cases a reducing sugar. But the best known and constant products of its decomposition are

Phosphoric acid.

Purine bases, viz.:
Adenine.
Hypoxanthine.
Guanine.
Xanthine.

The nuclein obtained from the nuclei or heads of the spermatozoa consists of nucleic acid without any proteid admixture. In fishes' spermatozoa, however, the nucleic acid is united to protamine, the chemical properties of which we shall be considering immediately.

C. ALBUMINOIDS.

The **albuminoids** are a group of substances which, though similar to the proteids in many particulars, differ from them in certain other points. The principal members of the group are the following:—

Collagen, the substance of which the white fibres of connective-tissue are composed. Some observers regard it as the anhydride of gelatin. In bone it is often called *ossein.*

Gelatin.—This substance is produced by boiling collagen with water. It possesses the peculiar property of setting into a jelly when a solution made with hot water cools. It gives most of the proteid colour tests. Most observers state, however, that it contains very little sulphur. On digestion it is like proteid converted into peptone-like substances, and is readily absorbed. Though it will replace in diet a certain quantity of proteid, acting as what is called a 'proteid-sparing' food, it cannot altogether take the place of proteid as a food. Animals fed on gelatin instead of proteid waste rapidly.

Chondrin, the very similar substance obtained from hyaline cartilage, is a mixture of gelatin with mucinoid materials.

Elastin.—This is the substance of which the yellow or elastic fibres of connective-tissue are composed. It is a very insoluble material. The sarcolemma of muscular fibres and certain basement membranes are very similar.

Keratin, or horny material, is the substance found in the surface layers of the epidermis, in hairs, nails, hoofs, and horns. It is very insoluble, and chiefly differs from proteids in its high percentage of sulphur. A similar substance, called *neurokeratin*, is found in neuroglia and nerve-fibres. In this connection it is interesting to note that the epidermis and the nervous system are both formed from the same layer of the embryo—the epiblast.

Chitin and similar substances found in the exoskeleton of many invertebrates.

D. THE PROTAMINES.

Protamines.—These are basic substances which are combined with nuclein in the heads of the spermatozoa of certain fishes (salmon, sturgeon, etc.). They resemble proteids in many of their characters; *e.g.*, they give Piotrowski's reaction and some of the other tests for proteids. They are regarded by Kossel as the simplest proteids. By decomposition in various ways they yield bases containing six atoms of carbon, and called in consequence the *hexone* bases; the bases are named lysine ($C_6H_{14}N_2O_2$), arginine ($C_6H_{14}N_4O_2$), and histidine ($C_6H_9N_3O_2$).

The more complex proteids and albuminoids yield these bases also; therefore Kossel considers that all these substances contain a protamine nucleus. The more complex proteids, however, yield many other products of decomposition in addition to these bases, such as leucine and tyrosine.

The Polarimeter.

This instrument is one by means of which the action of various substances on the plane of polarised light can be observed and measured.

Most of the carbohydrates are dextro-rotatory.

All the proteids are levo-rotatory.

There are many varieties of the instrument; these can only be properly studied in a practical class, and all one can do here is to state briefly the principles on which they are constructed.

Suppose one is shooting arrows at a fence made up of narrow vertical palings; suppose also that the arrows are flat like the laths of a Venetian blind. If the arrows are shot vertically they will pass easily through the gaps between the palings, but if they are shot horizontally they will be unable to pass through at all. This rough illustration will help us in understanding what is meant by polarised light. Ordinary light is produced by the undulations of æther occurring in all directions at right angles to the path of propagation of the wave. Polarised light is produced by undulations in one plane only; we may compare it to our flat arrows.

In a polarimeter, there is at one end of the instrument a Nicol's prism, which is made of Iceland spar. This polarises the light which passes through it; it is called the polariser. At the other end of the instrument is another called the analyser. Between the two is a tube which can be filled with fluid. If the analyser is parallel to the polariser the light will pass through to the eye of the observer. But if the analyser is at right angles to the polariser it is like the flat arrows hitting horizontally the vertical palings of the fence, and there is darkness. At intermediate angles there will be intermediate degrees of illumination.

If the analyser and polariser are parallel and the intermediate tube filled with water, the light will pass as usual, because water has no action on the plane of polarised light. But if the water contains sugar or some "optically active" substance in solution the plane is twisted in one direction or the other according as the substance is dextro- or levo-rotatory. The amount of rotation is measured by the number of angles through which the analyser has to be turned in order to obtain the full illumination. This will vary with the length of the tube and the strength of the solution.

Ferments.

The word **fermentation** was first applied to the change of sugar into alcohol and carbonic acid by means of yeast. The evolution of carbonic acid causes frothing and bubbling; hence the term "fermentation." The agent, yeast, which produces this, is called the ferment. Microscopic investigation shows that yeast is composed of minute rapidly-growing unicellular organisms (torulæ) belonging to the fungus group of plants.

The souring of milk, the transformation of urea into ammonium carbonate in decomposing urine, and the formation of vinegar (acetic acid) from alcohol are brought about by very similar organisms. The complex series of changes known as putrefaction, which are accompanied by the formation of malodorous gases, and which are produced by the various forms of bacteria, also come into the same category.

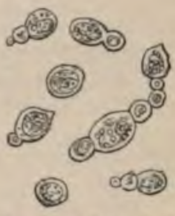


FIG. 342.—Cells of the yeast plant in process of budding.

That the change or fermentation is produced by these organisms is shown by the fact that it occurs only when the organisms are present, and stops when they are removed or killed by a high temperature or by certain substances (carbolic acid, mercuric chloride, etc.) called antiseptics.

The "germ theory" of disease explains the infectious diseases by considering that the change in the system is of the nature of fermentation, and, like the others we have mentioned, produced by microbes; the transference of the bacteria or their spores from one person to another constitutes infection. The poisons produced by the growing bacteria appear to be either alkaloidal (ptomaines) or proteid in nature. The existence of poisonous proteids is a very remarkable thing, as no chemical differences can be shown to exist between them and those which are not poisonous, but which are useful as foods. The most virulent poison in existence, namely snake poison, is a proteid of the proteose class.

There is another class of chemical transformations which at first sight differ very considerably from all of these. They, however, resemble these fermentations in the fact that they occur independently of any apparent change in the agents that produce them. The agents that produce them are not living organisms, but chemical substances, the result of the activity of living cells. The change of starch into sugar by the ptyalin of the saliva is an instance.

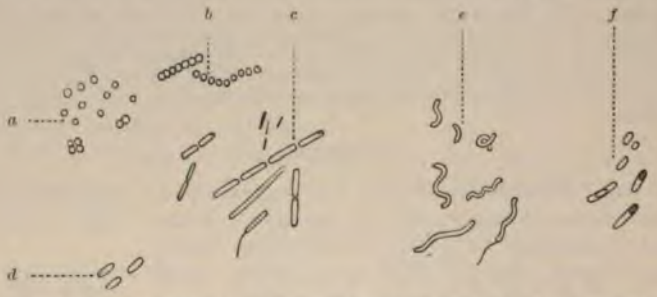


FIG. 343.—Types of micro-organisms: *a*, micrococci arranged singly; in twos, diplococci—if all the micrococci at *a* were grouped together they would be called staphylococci—and in fours, sarcinæ; *b*, micrococci in chains, streptococci; *c* and *d*, bacilli of various kinds (one is represented with a flagellum); *e*, various forms of spirilla; *f*, spores, either free or in bacilli.

Ferments may therefore be divided into two classes:—

1. The organised ferments—torulæ, bacteria, etc.
2. The unorganised ferments, or enzymes—like ptyalin.

The distinction between organised ferments and enzymes is, however, more apparent than real; for the micro-organisms exert their action by enzymes which they secrete. This has long been known in connection with the invertin of yeast, and for the enzyme secreted by the micrococcus ureæ, which converts urea into ammonium carbonate. In recent years Buchner, by crushing yeast cells, succeeded in obtaining from them an enzyme which produces the alcoholic fermentation, and there is no doubt that what is true for yeast is equally true for all the organised ferments, and in several cases this has been already proved experimentally.

The unorganised ferments may be classified as follows:—

(*a*) Amylolytic—those which change amyloses (starch, glycogen) into sugars. Examples: ptyalin, diastase, amylopsin.

(*b*) Proteolytic—those which change proteids into proteoses and peptones. Examples: pepsin, trypsin.

(*c*) Steatolytic—those which split fats into fatty acids and glycerin. An example, steapsin, is found in pancreatic juice.

(*d*) Inversive — those which convert saccharoses (cane sugar, maltose, lactose) into glucose. Examples: invertin of intestinal juice and of yeast cells.

(*e*) Coagulative—those which convert soluble into insoluble proteids. Examples: rennet, fibrin ferment.

Most ferment actions are hydrolytic—*i.e.*, water is added to the material acted on, which then splits into new materials. This is seen by the following examples:—

1. Conversion of cellulose into carbonic acid and marsh gas (methane) by putrefactive organisms—

$$\underset{\text{[Cellulose.]}}{(C_6H_{10}O_5)n} + \underset{\text{[Water.]}}{nH_2O} = \underset{\text{[Carbonic acid.]}}{3nCO_2} + \underset{\text{[Methane.]}}{3nCH_4}.$$

2. Inversion of cane sugar by the unorganised ferment invertin—

$$\underset{\text{[Cane sugar.]}}{C_{12}H_{22}O_{11}} + \underset{\text{[Water.]}}{H_2O} = \underset{\text{[Dextrose.]}}{C_6H_{12}O_6} + \underset{\text{[Levulose.]}}{C_6H_{12}O_6}.$$

Some enzymes, called *oxidases*, are oxygen carriers, and produce oxidation. They occur in living tissues.

A remarkable fact concerning the ferments is that the substances they produce in time put a stop to their activity; thus, in the case of the organised ferments, the alcohol produced by yeast, the phenol, cresol, etc., produced by putrefactive organisms from proteids, first stop the growth of and ultimately kill the organisms which produce them. In the case of the enzymes also the products of their activity hinder and finally stop their action, but on the removal of these products the ferments resume work.

This fact suggested to Croft Hill the question whether ferments will act in the reverse manner to their usual action; and in the case of one ferment, at any rate, he found this to be the case. Inverting ferments, as we have just seen, usually convert a disaccharide into monosaccharides. One of these inverting ferments, called *maltase*, converts maltose into dextrose. If the ferment is allowed to act on strong solutions of dextrose, it converts a small proportion of that sugar back into maltose again. This discovery of Croft Hill's has since been confirmed by others in relation to other enzymes.

Ferments act best at a temperature of about 40° C. Their activity is stopped, but the ferments are not destroyed, by cold; it is stopped and the ferments killed by too great heat. A certain amount of moisture and oxygen is also necessary; there are, however, certain micro-organisms that act without free oxygen, and are called anaërobic in contradistinction to those which require oxygen, and are called aërobic.

The chemical nature of the enzymes, or unorganised ferments, is very difficult to investigate; they are substances that elude the grasp of the chemist to a great extent. So far, however, research has taught us that they are either proteid in nature or are substances closely allied to the proteids.

CHAPTER XXVI

THE BLOOD

THE blood is the fluid medium by means of which all the tissues of the body are directly or indirectly nourished; by means of it also such of the materials resulting from the metabolism of the tissues which are of no further use in the economy are carried to the excretory organs. It is a somewhat viscid fluid, and in man and in all other vertebrate animals, with the exception of two,* is red in colour. It consists of a yellowish fluid, called **plasma** or **liquor sanguinis**, in which are suspended numerous **blood corpuscles**, which are, for the most part, coloured, and it is to their presence that the red colour of the blood is due.

Even when examined in very thin layers, blood is *opaque*, on account of the different refractive powers possessed by its two constituents, viz., the plasma and the corpuscles. On treatment with ether, water, and other reagents, however, it becomes transparent and assumes a lake colour, in consequence of the colouring matter of the corpuscles having been discharged into the plasma. The average *specific gravity* of blood at 15° C. (60° F.) varies from 1055 to 1062. A rapid and useful method of estimating the specific gravity of blood was invented by Roy. Drops of blood are taken and allowed to fall into fluids of known specific gravity. When the drop neither rises nor sinks in the fluid it is taken to be of the same specific gravity as that of the standard fluid. The *reaction* of blood is faintly alkaline and the *taste* saltish. Its *temperature* varies slightly, the average being 37·8° C. (100° F.). The blood-stream is warmed by passing through the muscles, nerve centres, and glands, but is somewhat cooled on traversing the capillaries of the skin. Recently drawn blood has a distinct *odour*, which in many cases is characteristic of the animal from which it has been taken; it may be further developed by adding to blood a mixture of equal parts of sulphuric acid and water.

Quantity of the Blood.—The quantity of blood in any animal under normal conditions bears a fairly constant relation to the body-weight. The methods employed for estimating it are not so simple as might at first sight have been thought. For example, it would not be possible to get any accurate information on the point from the amount obtained by rapidly bleeding an animal to death, for then an indefinite quantity would remain in the vessels; nor, on the other hand, would it be possible to obtain a correct estimate by less rapid bleeding, as, since life would be more prolonged, time would be allowed for the passage into the blood of lymph from the lymphatic vessels and from the tissues. In the former case, therefore, we should under-estimate, and in the latter over-estimate, the total amount of the blood.

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* The *amphioxus* and the *leptocephalus*.

The method usually employed is the following:—A small quantity of blood is taken from an animal by venesection; it is defibrinated and measured, and used to make standard solutions of blood. The animal is then rapidly bled to death, and the blood which escapes is collected. The blood-vessels are next washed out with saline solution until the washings are no longer coloured, and these are added to the previously withdrawn blood; lastly, the whole animal is finely minced with saline solution. The fluid obtained from the mincings is carefully filtered and added to the diluted blood previously obtained, and the whole is measured. The next step in the process is the comparison of the colour of the diluted blood with that of standard solutions of blood and water of a known strength, until it is discovered to what standard solution the diluted blood corresponds. As the amount of blood in the corresponding standard solution is known, as well as the total quantity of diluted blood obtained from the animal, it is easy to calculate the absolute amount of blood which the latter contained, and to this is added the small amount which was withdrawn to make the standard solutions. This gives the total amount of blood which the animal contained. It is contrasted with the weight of the animal, previously known. The result of experiments performed in this way showed that the quantity of blood in various animals differs a good deal, but in the dog averages $\frac{1}{12}$ to $\frac{1}{14}$ of the total body-weight.

An estimate of the quantity in man which corresponded nearly with this proportion has been more than once made from the following data. A criminal was weighed before and after decapitation; the difference in the weight represented the quantity of blood which escaped. The blood-vessels of the head and trunk were then washed out by the injection of water until the fluid which escaped had only a pale red or straw colour. This fluid was also weighed; and the amount of blood which it represented was calculated by comparing the proportion of solid matter contained in it with that of the first blood which escaped on decapitation. (Weber and Lehmann.)

Haldane and Lorrain Smith have recently investigated the question by another method. The data required are (1) the percentage of hæmoglobin in the blood, and (2) the extent to which the hæmoglobin is saturated by a *measured* amount of carbonic oxide absorbed into the blood.

The percentage of hæmoglobin is determined colorimetrically by the Gowers' or Gowers'-Haldane hæmoglobinometer (see p. 438). In the latter instrument the standard 100 per cent. of colour corresponds to a capacity of 18·5 c.c. of oxygen or carbonic oxide per 100 c.c. of blood. The subject whose blood is to be measured breathes a known volume of carbonic oxide, and a few drops of the blood are taken and the saturation of his hæmoglobin is determined colorimetrically. From this result the total capacity of the blood for carbonic oxide is calculated. The "carbonic oxide capacity" is the same as the "oxygen capacity." The volume of the blood is then calculated from the total "oxygen capacity," and the percentage capacity as determined by the hæmoglobinometer. The following is an example:—The subject's blood in a given case has, let us say, the colour of the 100 per cent. standard, and therefore has a capacity of 18·5 c.c. per 100 c.c. blood. He is then allowed to breathe 75 c.c. of carbonic oxide, and it is then found that his blood is 15 per cent. saturated. The amount required to completely saturate his blood, or in other words his total capacity, must be $75 \times \frac{100}{15} = 500$ c.c. Since 18·5 c.c. of this total is carried by 100 c.c. of his blood, the total volume required to contain 500 c.c. is $500 \times \frac{100}{18{\cdot}5} = 2700$ c.c. The subject has therefore 2·7 litres of blood. The total weight is obtained by multiplying the volume by the specific gravity (about 1·055).

Some of the results of this method are as follows:—The mass of the blood in man is about 4·9 per cent. $\left(\frac{1}{20{\cdot}5}\right)$ of the body-weight. The corresponding ratio of the blood volume is 4·62 c.c. per 100 grammes or $\frac{1}{21{\cdot}6}$. The commonly accepted estimate of the mass of the blood is thus too high. In pathological conditions the numbers are different; thus in anæmia from hæmorrhage, the volume ratio is 6·5, in pernicious anæmia 8·6, in chlorosis 10·8. In other words, in various forms of anæmia the actual volume of the blood is increased. Prof. Lorrain Smith has pointed out to me that the decapitated criminal investigated by Weber and Lehmann mentioned above, suffered from scurvy, a disease which is accompanied by anæmia; hence the total volume of his blood was pathologically high.

Coagulation of the Blood.

One of the most characteristic properties which the blood possesses is that of *clotting* or *coagulating*. This phenomenon may be observed under the most favourable conditions in blood which has been drawn into an open vessel. In about two or three minutes, at the ordinary temperature of the air, the surface of the fluid is seen to become semi-solid or *jelly-like*, and this change takes place in a minute or two afterwards at the sides of the vessel in which it is contained, and then extends throughout the entire mass. The time which is occupied in these changes is about eight or nine minutes. The solid mass is of exactly the same volume as the previously liquid blood, and adheres so closely to the sides of the containing vessel that if the latter is inverted none of its contents escape. The solid mass is the *crassamentum*, or *clot*. If the clot is watched for a few minutes, drops of a light straw-coloured fluid, the *serum*, may be seen to make their appearance on the surface, and, as they become more and more numerous, to run together, forming a complete superficial stratum above the solid clot. At the same time the fluid begins to transude at the sides and at the under-surface of the clot, which in the course of an hour or two floats in the liquid. The first drops of serum appear on the surface about eleven or twelve minutes after the blood has been drawn; and the fluid continues to transude for from thirty-six to forty-eight hours.

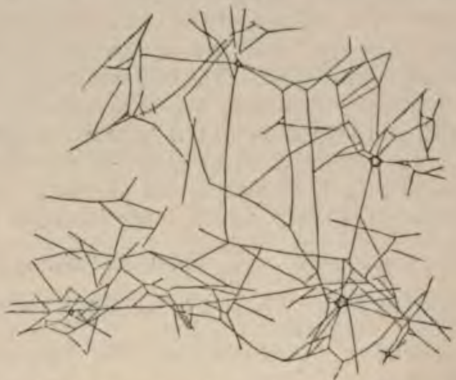

FIG. 344.—Reticulum of fibrin, from a drop of human blood, after treatment with rosanilin. The entangled corpuscles are not seen. (Ranvier.)

The clotting of blood is due to the development in it of a substance called *fibrin*, which appears as a meshwork (fig. 344) of fine fibrils. This meshwork entangles and encloses within itself the blood corpuscles. The first clot formed, therefore, includes the whole of the constituents of the blood in an apparently solid mass, but soon the fibrinous meshwork begins to contract, and the serum which does not belong to the clot is squeezed out. When the whole of the serum has transuded the clot is found to be smaller, but firmer, as it is now made up chiefly of fibrin and blood corpuscles. Thus coagulation re-arranges the constituents of the blood; liquid blood is made up of plasma and blood corpuscles, and clotted blood of serum and clot.

Fibrin is formed from the plasma, and may be obtained free from corpuscles when blood-plasma is allowed to clot, the corpuscles having previously been removed. It may be also obtained from blood by whipping it with a bunch of twigs; the fibrin adheres to the twigs and entangles but few corpuscles. These may be removed by washing with water. Serum is plasma *minus* fibrin. The relation of plasma, serum, and clot can be seen at a glance in the following scheme of the constituents of the blood:—

$$\text{Blood}\left\{\begin{array}{l}\text{Plasma}\;\left\{\begin{array}{l}\text{Serum}\\ \text{Fibrin}\end{array}\right.\\ \\ \\ \text{Corpuscles}\end{array}\right.\left.\begin{array}{l}\\ \\ \\ \\ \end{array}\right\}\text{Clot}$$

It may be roughly stated that in 100 parts by weight of blood 60-65 parts consist of plasma and 35-40 of corpuscles.

The *buffy coat* is seen when blood coagulates slowly, as in horse's blood. The red corpuscles sink more rapidly than the white, and the upper stratum of the clot (buffy coat) consists mainly of fibrin and white corpuscles.

Coagulation is hastened by—

1. A temperature a little over that of the body.
2. Contact with foreign matter.
3. Injury to the vessel walls.
4. Agitation.
5. Addition of calcium salts.

Coagulation is hindered or prevented by—

1. A low temperature. In a vessel cooled by ice, coagulation may be prevented for an hour or more.
2. The addition of a large quantity of neutral salts like sodium sulphate or magnesium sulphate.
3. Contact with the living vascular walls.
4. Contact with oil.
5. Addition of soluble oxalates. These precipitate the calcium necessary for coagulation as insoluble calcium oxalate. Sodium fluoride or citrate may be used instead of the oxalate.
6. Injection of commercial peptone (which consists chiefly of proteoses) into the circulation of the living animal.

7. Addition of leech extract. This acts in virtue of a proteose it contains.

The theory generally received which accounts best for the coagulation of the blood is that of Hammarsten, and it may be briefly stated as follows:

When blood is in the vessels one of the constituents of the plasma, a proteid of the globulin class called fibrinogen, exists in a soluble form.

When the blood is shed the fibrinogen molecule is split into two parts: one part is a globulin, which remains in solution; the other is the insoluble material fibrin.

This change is brought about by the activity of a special unorganised ferment called the fibrin-ferment or thrombin.

This ferment does not exist in healthy blood contained in healthy blood-vessels, but is one of the products of the disintegration of the white corpuscles and blood platelets that occurs when the blood leaves the vessels or comes into contact with foreign matter.

To this it may be added, as the result of recent research, that a soluble calcium salt is essential for the formation of the ferment; that the fibrin-ferment belongs to the class of nucleo-proteids; that other nucleo-proteids (Wooldridge's tissue-fibrinogens) obtained from most of the cellular organs of the body produce intravascular clotting when injected into the circulation of a living animal.

The substance which is converted into fibrin-ferment or thrombin by the action of a calcium salt may be conveniently termed *prothrombin.*

The process of fibrin formation may therefore be represented in the following tabular way:—

In the plasma a proteid substance exists, called—
FIBRINOGEN.

From the colourless corpuscles a nucleo-proteid is shed out, called—
PROTHROMBIN.

By the action of calcium salts prothrombin is converted into fibrin-ferment, or
THROMBIN.

Thrombin acts on fibrinogen in such a way that two new substances are formed.

One of these is unimportant, viz., a globulin (*fibrino-globulin*) which remains in solution. Its amount is very small.

The other is important, viz., FIBRIN, which entangles the corpuscles and so forms the CLOT.

The Plasma and Serum.

The liquid in which the corpuscles float may be obtained by employing one or other of the methods already described for preventing the blood from coagulating. The corpuscles, being heavy, sink, and the supernatant plasma can then be removed by a pipette or siphon, or more thoroughly by the use of a centrifugal machine (see fig. 345).

On counteracting the influence which has prevented the blood from coagulating, the plasma then itself coagulates. Thus plasma obtained by the use of cold clots on warming gently; plasma which has been decalcified by the action of a soluble oxalate clots on the addition of a calcium salt; plasma obtained by the use of a strong solution of salt coagulates when this is diluted by the addition of water, the addition of fibrin-ferment being necessary in most cases; where coagulation occurs without the addition of fibrin-ferment no doubt some is present from the partial disintegration of the corpuscles

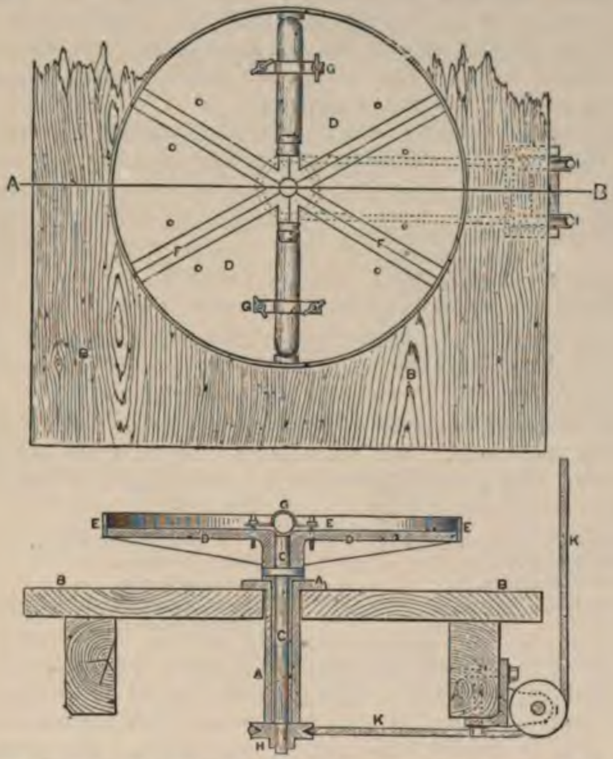

FIG. 345.—Plan and section of centrifugal machine. A, an iron socket secured to top of table B; C, a steel spindle carrying the turntable D, and turning freely in A; E, a flange round turntable D; F F, shallow grooves on face of D in which the test tubes are fixed by clamps G G; H, a pulley fixed to end of spindle C, and turned by the cord K; I I are two guide pulleys for cord K. The upper part of the figure is a surface view of the rotating turntable. (Gamgee.)

which has already occurred. Pericardial and hydrocele fluids resemble pure plasma very closely in composition. As a rule, however, they contain few or no white corpuscles, and do not clot spontaneously, but after the addition of fibrin-ferment, or liquids like serum that contain fibrin-ferment, they always yield fibrin.

Pure plasma may be obtained from horse's veins by what is known as the "living test-tube" experiment. If the jugular vein is ligatured in two places so as to include a quantity of blood within it, then removed from the animal and hung in a cool place, the blood will not clot for many hours. The corpuscles settle, and the supernatant plasma can be removed with a pipette.

The plasma is alkaline, yellowish in tint, and its specific gravity is about 1026 to 1029. 1000 parts of plasma contain :—

Water	902·90
Solids	97·10
Proteids : 1. yield of fibrin	4·05
2. other proteids	78·84
Extractives (including fat)	5·66
Inorganic salts	8·55

In round numbers, plasma contains 10 per cent. of solids, of which 8 are proteid in nature. Note, however, the comparatively small yield of fibrin.

Serum contains the same three classes of constituents—proteids, extractives, and salts. The extractives and salts are the same in both liquids. The proteids are different, as is shown in the following table :—

Proteids of Plasma.	*Proteids of Serum.*
Fibrinogen.	Serum globulin.
Serum globulin.	Serum albumin.
Serum albumin.	Fibrin-ferment (nucleo-proteid).
	Fibrino-globulin.

The gases of plasma and serum are small quantities of oxygen, nitrogen, and carbonic acid. The greater part of the oxygen of the blood is combined in the red corpuscles with hæmoglobin; the carbonic acid is chiefly combined as carbonates. The gases of the blood have already been considered under Respiration (see p. 378).

We may now study one by one the various constituents of the plasma and serum.

A. **Proteids.**—*Fibrinogen.* This is the substance acted on by fibrin-ferment. It yields, under this action, an insoluble product called *fibrin*, and a soluble proteid of the globulin class (fibrino-globulin).

Fibrinogen is a globulin. It differs from serum globulin, and may be separated from it, by making use of the fact that half-saturation with sodium chloride precipitates it. It coagulates by heat at the low temperature of 56° C.

Serum globulin and serum albumin.—These substances exhibit the usual differences already described between albumins and globulins (p. 400). Both are coagulated by heat at a little over 70° C. They may be separated by dialysis or the use of neutral salts.* The readiest way to separate them is to add to the serum an equal volume of saturated solution of ammonium sulphate. This is equivalent to semi-saturation, and it precipitates the globulin. If magnesium sulphate is used as a precipitant of the globulin it must be added in the form of crystals, and the mixture well shaken to ensure complete saturation.

Serum globulin was formerly called *fibrinoplastin*, because it was believed to take some share in fibrin formation. It is also called *paraglobulin*. It may be imperfectly precipitated by diluting serum with twenty times its volume of water and then adding a little dilute acetic acid, or passing a stream of carbonic acid gas through the diluted serum.

Fibrin-ferment.—Schmidt's method of preparing it is to take serum and add excess of alcohol. This precipitates all the proteids, fibrin-ferment included. After some weeks the alcohol is poured off; the serum globulin and serum albumin have been by this means rendered insoluble in water; an aqueous extract is, however, found to contain fibrin-ferment, which is not so easily coagulated by alcohol as the other proteids are.

B. **Extractives.**—These are non-nitrogenous and nitrogenous. The non-nitrogenous are fats, soaps, cholesterin, and sugar, the nitrogenous are urea (0·02 to 0·04 per cent.), and still smaller quantities of uric acid, creatine, creatinine, xanthine, and hypoxanthine.

C. **Salts.**—The most abundant salt is sodium chloride; it constitutes between 60 and 90 per cent. of the total mineral matter. Potassium chloride is present in much smaller amount. It constitutes about 4 per cent. of the total ash. The other salts are phosphates and sulphates.

Schmidt gives the following table:—

1000 parts of plasma yield—	
Mineral matter	8·550
Chlorine	3·640
SO_3	0·115
P_2O_5	0·191
Potassium	0·323
Sodium	3·341
Calcium phosphate	0·311
Magnesium phosphate	0·222

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* The globulin of the serum precipitated by "salting out" really consists of two proteids, one of which is precipitated by dialysis (euglobulin), and the other is not (pseudo-globulin).

The Blood-Corpuscles.

There are two principal forms of corpuscles, the *red* and the *white*, or, as they are now frequently named, the *coloured* and the *colourless*. In the moist state the red corpuscles form about 40 per cent. by weight of the whole mass of the blood. The proportion of colourless corpuscles is only as 1 to 500 or 600 of the coloured.

Red or Coloured Corpuscles.—Human red blood corpuscles are circular biconcave discs with rounded edges, $\frac{1}{3200}$ inch in diameter (7μ to 8μ) and $\frac{1}{12000}$ inch, or about 2μ, in thickness. When viewed singly they appear of a pale yellowish tinge; the deep red colour which they give to the blood is observable in them only when they are seen *en masse*.

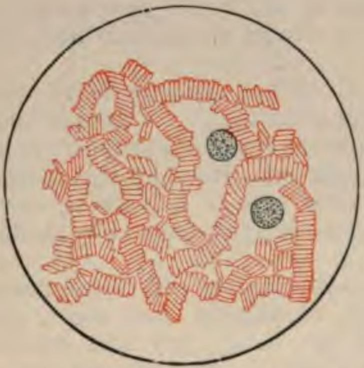


Fig. 346.—Red corpuscles in rouleaux. The white corpuscles are uncoloured.

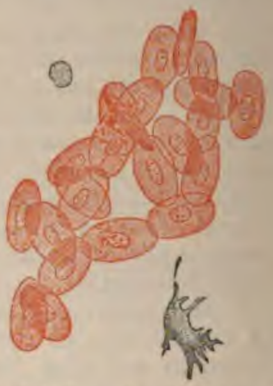


Fig. 347.—Corpuscles of the frog. The central mass consists of nucleated coloured corpuscles. The other corpuscles are two varieties of the colourless form.

According to Rollett they are composed of a transparent filmy framework infiltrated in all parts by the red pigment *hæmoglobin*. This *stroma* is elastic, so that as the corpuscles circulate, they admit of change in form, and recover their natural shape as soon as they escape from compression. According to this theory, the consistency of the peripheral part of the stroma is greater than that of the central portions; the outer layer thus plays the part of a membrane in the processes of osmosis that occur when water or salt solutions are added to the corpuscles. This view of Rollett has been questioned, particularly by Schäfer, who regards the red corpuscles as composed of a colourless envelope enclosing a solution of hæmoglobin. The presence of a membrane on the exterior of the corpuscle is undoubted, and can be clearly distinguished by a good microscope in the larger corpuscles of amphibia. It is, however, difficult to explain the elasticity of the corpuscles, and the central position of the nucleus in nucleated red corpuscles, unless we also assume that delicate fibres pass across the interior of the corpuscles.

Mammalian red corpuscles have no nuclei; the unequal refraction of transmitted light gives the appearance of a central spot, darker or brighter than the border, according as it is viewed in or out of focus. Their specific gravity is about 1088.

The corpuscles of all mammals, with the exception of the camel tribe, are circular and biconcave. They are generally very nearly the size of human red corpuscles. They are smallest in the deer tribe and largest in the elephant. In the camelidæ they are biconvex. In all mammals the corpuscles are non-nucleated, and in all other vertebrates (birds, reptiles, amphibia, and fishes) the corpuscles are oval, biconvex, and nucleated (fig. 348) and larger than in mammals. They are largest of all in certain amphibians (*amphiuma, proteus*).

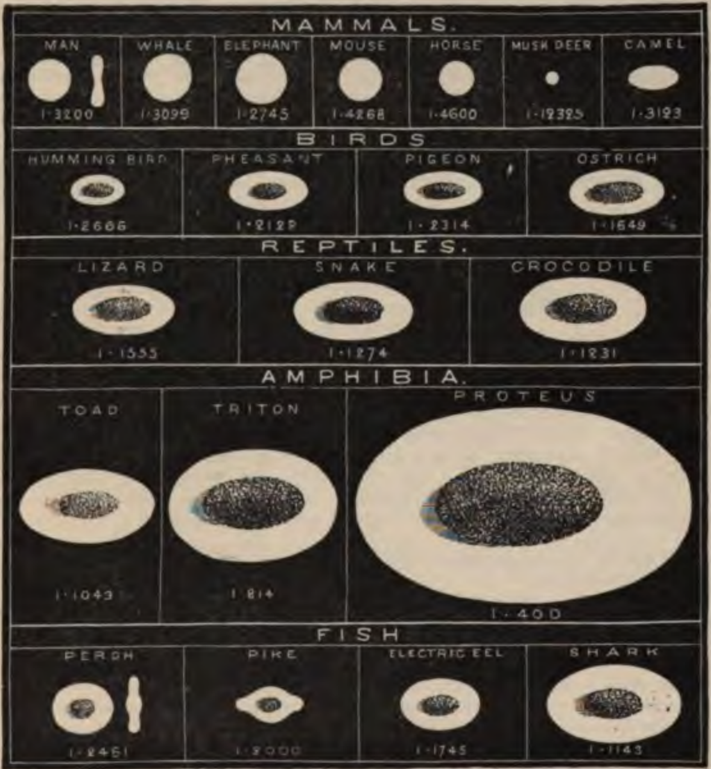


FIG. 348.—The above illustration is somewhat altered from a drawing by Gulliver, in the Proceed. Zool. Society, and exhibits the typical characters of the red blood-cells in the main divisions of the Vertebrata. The fractions are those of an inch, and represent the average diameter. In the case of the oval cells, only the long diameter is here given. It is remarkable, that although the size of the red blood-cells varies so much in the different classes of the vertebrate kingdom, that of the white corpuscles remains comparatively uniform, and thus they are, in some animals, larger, in others smaller, than the red corpuscles.

The red corpuscles are not all alike, for in almost every specimen of blood may be also observed a certain number of corpuscles smaller than the rest. They are termed *microcytes*, or *hæmatoblasts*, and are probably immature corpuscles.

A property of the red corpuscles, which is exaggerated in inflammatory blood, is a tendency to adhere together in rolls or columns (rouleaux), like piles of coins. These rolls quickly fasten together by their ends, and cluster; so that, when the blood is spread out thinly on a glass they form an irregular network (fig. 346).

Action of Reagents.—Considerable light has been thrown on the physical and chemical constitution of red blood-cells by studying the effects produced by mechanical means and by various reagents; the following is a brief summary of these reactions:—

Water.—When water is added gradually to frog's blood, the oval disc-shaped corpuscles become spherical, and gradually discharge their hæmoglobin, a pale, transparent stroma or envelope being left behind: human red blood-cells swell, change from a discoidal to a spheroidal form, and discharge their pigment, becoming quite transparent and all but invisible. This effect is due to osmosis.

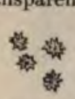


FIG. 349.—Effect of saline solution (crenation).

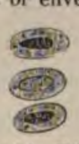


FIG. 350.—Effect of acetic acid.

Physiological saline solution causes no effect on the red corpuscles beyond preventing them running into rouleaux. If a stronger salt solution is used, the corpuscles shrink and become crenated (fig. 349) owing to osmosis of water outwards.

Dilute acetic acid causes the nucleus of the red blood-cells in the frog to become more clearly defined; if the action is prolonged, the nucleus becomes strongly granulated, and all the colouring matter seems to be concentrated in it, the surrounding cell-substance and outline of the cell becoming almost invisible; after a time the cells lose their colour altogether. The cells in the figure (fig. 350) represent the successive stages of the change. A similar loss of colour occurs in the red corpuscles of human blood, which, however, from the absence of nuclei, seem to disappear entirely.

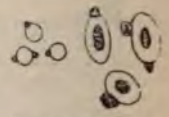


FIG. 351.—Effect of tannin.

Dilute alkalis cause the red blood-cells to dissolve slowly, and finally to disappear.

Chloroform, *ether*, and other reagents that dissolve fats dissolve the fatty substance (lecithin, etc.) of the membrane that surrounds the corpuscles, and so produce laking of the blood.

Tannic acid.—When a 2 per cent. fresh solution of tannic acid is applied to frog's blood it causes the appearance of a sharply-defined little knob, projecting from the free surface (*Roberts' macula*): the colouring matter becomes at the same time concentrated in the nucleus, which grows more distinct (fig. 351). A somewhat similar effect is produced on the human red blood-corpuscle, the colouring matter being discharged and coagulated as a little knob of hæmatin on the surface of the corpuscle.

Boric acid.—A 2 per cent. solution applied to nucleated red blood-cells (frog) will cause the concentration of all the colouring matter in the nucleus; the coloured body thus formed gradually quits its central position, and comes to be partly, sometimes entirely, protruded from the surface of the now colourless cell (fig. 352). The result of this experiment led Brücke to distinguish the coloured contents of the cell (*zooid*) from its colourless stroma or envelope (*œcoid*). When applied to the non-nucleated mammalian corpuscle its effect merely resembles that of other dilute acids.

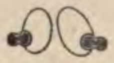


FIG. 352.—Effect of boric acid.

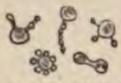


FIG. 353.—Effect of heat.

Heat.—The effect of heat up to 50°—60° C. (120°—140° F.) is to cause the formation of a number of bud-like processes.

Electricity causes the red blood-corpuscles to become crenated, and at length mulberry-like. Finally they recover their round form and become quite pale.

The Colourless Corpuscles.—In human blood the white or colourless corpuscles or *leucocytes* (when at rest) are nearly spherical masses of granular protoplasm. In all cases one or more nuclei exist in each corpuscle. The size of the corpuscles varies considerably, but averages $\frac{1}{2500}$ of an inch (10μ) in diameter.

In health, the proportion of white to red corpuscles, which, taking an average, is about 1 to 500 or 600, varies considerably even in the course of the same day. The variations appear to depend chiefly on the amount and probably also on the kind of food taken; the number of leucocytes is generally increased by a meal, and diminished by fasting. Also in young persons, during pregnancy, and after great loss of blood, there is a larger proportion of colourless blood-corpuscles. In old age, on the other hand, their proportion is diminished.

There are four principal varieties of colourless corpuscles found in human blood:—

1. *Poly-morpho-nuclear cells.*—These contain several nuclei united by fine threads of chromatin. Their protoplasm is filled with fine granules, which are termed *oxyphile* on account of their affinity for acid dyes like eosin. These are the most important leucocytes, constituting from 60 to 70 per cent. of the total.

2 *Eosinophile cells.*—These are not so actively amœboid as the first variety. Their nucleus is simple or lobed. Their protoplasmic granules are large, and are much more deeply stained by eosin than the fine granules of the first variety. They comprise about 5 per cent. of the total leucocytes.

3. *Lymphocytes.*—These have a large spherical nucleus and a limited amount of clear protoplasm around it. Transitional forms between them and the next variety are also found. They constitute from 15 to 30 per cent. of the total.

4. *Hyaline cells.*—These differ from the last by having more protoplasm around the nucleus. The protoplasm is amœboid, and is clear. It, however, stains slightly with methylene blue, and this is perhaps due to the presence of fine basophile granules.

The nuclei of all these varieties are basophile, *i.e.*, they have a strong affinity for basic aniline dyes like methylene blue. Cells, with large basophile granules, are very rare in healthy human blood.

Amœboid Movement.—The remarkable property of the colourless corpuscles of spontaneously changing their shape was first demonstrated by Wharton Jones in the blood of the skate. If a drop of blood is examined with a high power of the microscope, under conditions by which loss of moisture is prevented, and at the same time the temperature is maintained by a warm stage at about that of the body, 37° C. (98·5° F.), the colourless corpuscles will be observed slowly to alter their shapes, and to send out processes at various parts of their circumference. The amœboid movement, which can be demonstrated in human colourless blood-corpuscles, can be more readily seen in newt's blood.

The full consideration of amœboid movement is given on p. 12. An interesting variety of amœboid movement is that which leads to the ingestion of foreign particles. This gives to the leucocytes their power of taking in and digesting bacilli (*phagocytosis*). The multinucleated, finely granular corpuscles are the most vigorous phagocytes.

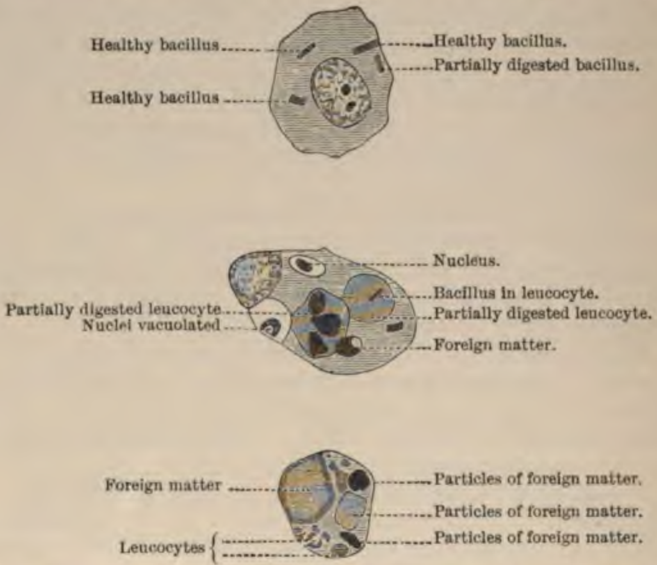

Healthy bacillus
Healthy bacillus.
Partially digested bacillus.
Healthy bacillus
Nucleus.
Bacillus in leucocyte.
Partially digested leucocyte
Partially digested leucocyte.
Nuclei vacuolated
Foreign matter.
Foreign matter
Particles of foreign matter.
Particles of foreign matter.
Particles of foreign matter.
Leucocytes

FIG. 354.—Macrophages containing bacilli and other structures undergoing digestion. (Ruffer.)

The accompanying figure illustrates this; the cells represented, however, are not leucocytes, but the large amœboid cells found in connective tissues, especially in inflamed parts.

The process of *emigration* of the leucocytes is described on p. 295.

Action of Reagents on the colourless corpuscles.—*Water* causes the corpuscles to swell and their nuclei to become apparent. *Acetic acid* (1 per cent.) has a similar action; it also causes the granules to aggregate round the nucleus. *Dilute alkalis* produce swelling and bursting of the corpuscles.

The Blood-Platelets.

Besides the two principal varieties of blood-corpuscles, a third kind has been described under the name blood-platelets (*Blut-plättchen*). These are colourless disc-shaped or irregular bodies, much smaller than red corpuscles. Different views are held as to their origin. At first they were regarded as immature red corpuscles; but this view has been discarded. Some state that they are merely a precipitate of nucleo-proteid which occurs when the plasma dies or is cooled. There is, however, no doubt that they do occur in living blood, and have been seen to undergo amœboid movement; some observers state that they are nucleated.

Enumeration of the Blood-Corpuscles.

Several methods are employed for counting the blood-corpuscles; most of them depend upon the same principle, *i.e.*, the dilution of a minute volume of blood with a given volume of a colourless saline solution similar in specific gravity to blood plasma, so that the size and shape of the corpuscles is altered as little as possible. A minute quantity of the well-mixed solution is then taken, examined under the microscope, either in a flattened capillary tube (Malassez) or in a cell (Hayem & Nachet, Gowers) of known capacity, and the number of corpuscles in a measured length of the tube, or in a given area of the cell, is counted. The length of the tube and the area of the cell are ascertained by means of a micrometer scale in the microscope ocular; or in the case of Gowers' modification, by the division of the cell area into squares of known size. Having ascertained the number of corpuscles in the diluted blood, it is easy to find out the number in a given volume of normal blood.

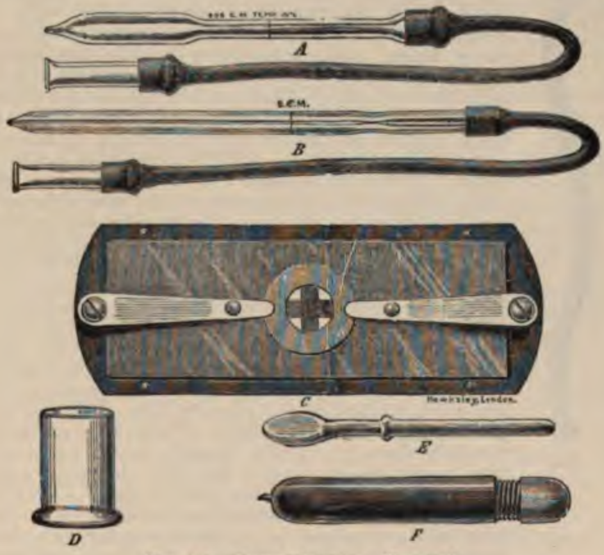


FIG. 355.—Hæmacytometer. (Gowers.)

Gowers' *Hæmacytometer* consists of a small pipette (A), which, when filled up to a mark on its stem holds 995 cubic millimetres. It is furnished with an indiarubber tube and glass mouth-piece to facilitate filling and emptying; a capillary tube (B) marked to hold 5 cubic millimetres, and also furnished with an indiarubber tube and mouth-piece; a small glass jar (D) in which the dilution of the blood is performed; a glass stirrer (E) for mixing the blood and salt solution thoroughly; (F) a needle, the length of which can be regulated by a screw; a brass stage plate (C) carrying a glass slide, on which is a cell one-fifth of a millimetre deep, and the bottom of which is divided into one-tenth millimetre squares. On the top of the cell a cover-slip rests. A standard saline solution of sodium sulphate, or similar salt, of specific gravity 1025, is made, and 995 cubic millimetres are measured by means of the pipette into the glass jar, and with this 5 cubic millimetres of blood, obtained by pricking the finger with the needle, and measured in the capillary pipette (B) are thoroughly mixed by the glass stirring-rod. A drop of this diluted blood is then placed in the cell and covered with a cover-slip, which is fixed in position by means of the two lateral springs. The layer of diluted blood between the slide and cover-glass is one-fifth of a millimetre thick. The preparation is then examined under a microscope with a power of about 400 diameters, and focussed until the lines dividing the cell into squares are visible.

FIG. 356.

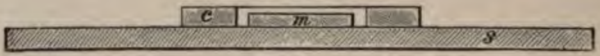
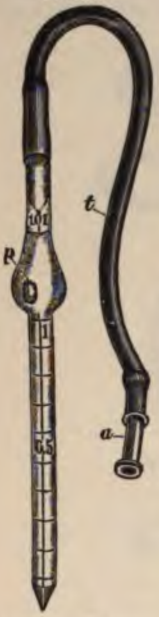


FIG. 357.



FIGS. 356 and 357.—Thoma-Zeiss Hæmacytometer.

After a short delay, the red corpuscles which have sunk to the bottom of the cell, and are resting on the squares, are counted in ten squares, and the number of white corpuscles noted. By adding together the numbers counted in ten (one-tenth millimetre) squares, and, as the blood has been diluted, multiplying by ten thousand, the number of corpuscles in one cubic millimetre of blood is obtained. The average number of corpuscles per cubic millimetre of healthy blood, according to Vierordt and Welcker, is 5,000,000 in adult men, and 4,500,000 in women; this corresponds to an average of 50 and 45 corpuscles respectively per square of Gowers' instrument.

A hæmacytometer of another form, and one that is much used at the present time, is known as the Thoma-Zeiss hæmacytometer. It consists of a carefully graduated pipette, in which the dilution of the blood is done; this is so formed that the capillary stem has a capacity equalling one-hundredth of the bulb above it. If the blood is drawn up in the capillary tube to the line marked 1 (fig. 357) the saline solution may afterwards be drawn up the stem to the line 101; in this way we have 101 parts, of which the blood forms 1. As the contents of the stem can be displaced unmixed we shall have in the mixture the proper dilution. The blood and the saline solution are well mixed by shaking the pipette, in the bulb of which is contained a small glass bead for the purpose of aiding the mixing. The other part of the instrument consists of a glass slide (fig. 356) upon which is mounted a covered disc, *m*, accurately ruled so as to present one square millimetre divided into 400 squares of one-twentieth of a millimetre each. The micrometer thus made is surrounded by another annular cell, *c*, which has such a height as to make the cell project exactly one-tenth millimetre beyond *m*. If a drop of the diluted blood is placed upon *m*, and *c* is covered with a perfectly flat cover-glass, the volume of the diluted blood above each of the squares of the micrometer, *i.e.*, above each $\frac{1}{400}$, will be $\frac{1}{4000}$ of a cubic millimetre. An average of ten or more squares is then taken, and this number multiplied by 4000 × 100 gives the number of corpuscles in a cubic millimetre of undiluted blood.

Dr George Oliver's Hæmacytometer is a much easier instrument to use, and the results obtained are accurate; it does not enable one, however, to ascertain the proportion of red and white corpuscles. A small measured quantity of blood is taken up into a pipette and washed out into a graduated flattened test-tube with Hayem's fluid (sodium chloride 0·5 gramme, sodium sulphate 0·25 gr., corrosive sublimate 0·25 gr., distilled water 100 c.c.). The graduations of the tube are so adjusted that with normal blood (*i.e.*, blood containing 5,000,000 red corpuscles per cubic millimetre) the light of a small wax candle placed three yards from the eye in a dark room, is just visible as a thin bright line when looked at through the tube held edgeways between the fingers, and filled up to the 100 mark with Hayem's fluid. If the number of corpuscles is less than normal, less of the diluting solution is required before the light is transmitted; if more than normal, more of the solution is necessary. The graduations of the tube correspond to percentages of the normal standard which is taken as 100.

Development of the Blood-Corpuscles.

The first formed blood-corpuscles of the human embryo differ much in their general characters from those which belong to the later periods of intra-uterine, and to all periods of extra-uterine, life. Their manner of origin is at first very simple.

Surrounding the early embryo is a circular area, called the vascular area, in which the first rudiments of the blood-vessels and blood-corpuscles are developed. Here the nucleated embryonic cells of the mesoblast, from which the blood-vessels and corpuscles are to be formed, send out processes in various directions, and these, joining together, form an irregular meshwork. The nuclei increase in number, and collect chiefly in the larger masses of protoplasm, but partly also in the processes. These nuclei gather around them a certain amount of the protoplasm, and, becoming coloured, form the red blood-corpuscles. The protoplasm of the cells and their branched network in which these corpuscles lie then become hollowed out into a system of canals enclosing fluid, in which the red nucleated corpuscles float. The corpuscles at first are from about $\frac{1}{2500}$ to $\frac{1}{1500}$ of an inch (10μ to 16μ) in diameter, mostly spherical, and with granular contents, and a well-marked nucleus. Their nuclei, which are about $\frac{1}{5000}$ of an inch (5μ) in diameter, are central and circular.

The corpuscles then strongly resemble the colourless corpuscles of the fully developed blood, but are coloured. They are capable of amœboid movement and multiply by division.

When, in the progress of embryonic development, the liver begins to be formed, the multiplication of blood-cells in the whole mass of blood ceases, and new blood-cells are produced by this organ, and also by the lymphatic glands, thymus and spleen. These are at first colourless and nucleated, but afterwards acquire the ordinary blood-tinge, and resemble very much those of the first set. They also multiply by division. In whichever way produced, however, whether from the original formative cells of the embryo, or by the liver and the other organs mentioned above, these coloured nucleated cells begin very early in fœtal life to be mingled with coloured *non*-nucleated corpuscles resembling those of the adult, and at about the fourth or fifth month of embryonic existence are completely replaced by them.

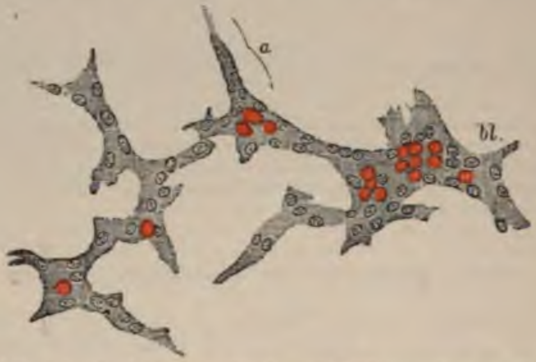


FIG. 358.—Part of the network of developing blood-vessels in the vascular area of a guinea-pig. *bl*, blood-corpuscles becoming free in an enlarged and hollowed-out part of the network; *a*, process of protoplasm. (E. A. Schäfer.)

Origin of the Matured Coloured Corpuscles.—The non-nucleated red corpuscles may possibly be derived from the nucleated, but in all probability are an entirely new formation. Their chief origin is:—

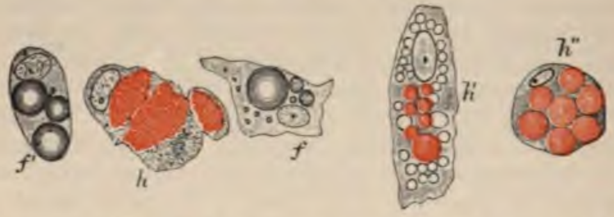


FIG. 359.—Development of red corpuscles in connective tissue cells. From the subcutaneous tissue of a new-born rat. *h*, a cell containing hæmoglobin in a diffused form in the protoplasm; *h′*, one containing coloured globules of varying size and vacuoles; *h″*, a cell filled with coloured globules of nearly uniform size; *f*, *f′*, developing fat cells. (E. A. Schäfer.)

From the medulla of bone.—It has been shown that coloured corpuscles are to a very large extent derived during adult life from the large pale cells in the red marrow of bones, especially of the ribs. These cells become coloured from the formation of hæmoglobin chiefly in one part of their protoplasm. This coloured part becomes separated from the rest of the cell and forms a red corpuscle, being at first cup-shaped, but soon taking on the normal appearance of the mature corpuscle. Mingled with the amœboid colourless marrow cells (p. 55) are a number of other smaller amœboid cells called *erythroblasts* (fig. 361); these are tinted with hæmoglobin; they divide and multiply, lose their nucleus, and are thus transformed into discoid blood-corpuscles.

From the tissue of the spleen.—It is probable that coloured as well as colourless corpuscles may be produced in the spleen from cells similar to the erythroblasts of red marrow.

The belief which formerly prevailed that the red corpuscles are derived from the white or from the platelets has now been discarded.

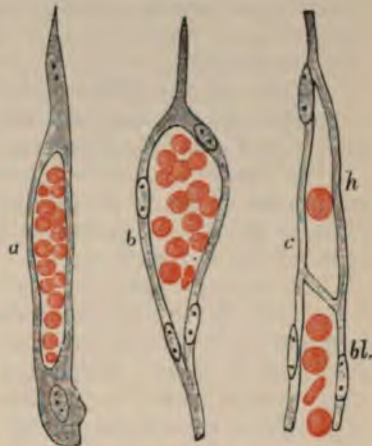


FIG. 360.—Further development of blood-corpuscles in connective tissue cells and transformation of the latter into capillary blood-vessels. *a*, an elongated cell with a cavity in the protoplasm occupied by fluid and by blood-corpuscles which are still globular; *b*, a hollow cell, the nucleus of which has multiplied. The new nuclei are arranged around the wall of the cavity, the corpuscles in which have now become discoid; *c*, shows the mode of union of a "hæmapoietic" cell, which, in this instance, contains only one corpuscle, with the prolongation (*bl*) of a previously existing vessel; *a* and *c*, from the new-born rat: *b*, from the fœtal sheep. (E. A. Schäfer.)

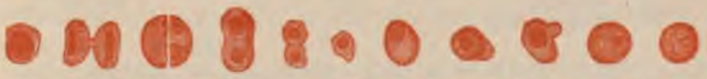


FIG. 361.—Coloured nucleated corpuscles, from the red marrow of the guinea-pig. (E. A. Schäfer.)

During fœtal life, and possibly in some animals, *e.g.* the rat, which are born in an immature condition, for some little time after birth, the blood discs have been stated by Schäfer to arise in the connective tissue cells in the following way. Small globules, of varying size, of colouring matter arise in the protoplasm of the cells (fig. 359), and the cells themselves become branched, their branches joining the branches of similar cells. The cells next become vacuolated, and the red globules are free in a cavity filled with fluid (fig. 360); by the extension of the cavity of the cells into their processes anastomosing vessels are produced, which ultimately join with the previously existing vessels, and the globules, now having the size and appearance of the ordinary red corpuscles, are passed into the general circulation. This method of formation is called *intracellular.* Without doubt, the red corpuscles have, like all other parts of the organism, a tolerably definite term of existence, and in a like manner die and waste away when the portion of work allotted to them has been performed. Neither the length of their life, however, nor the fashion of their decay, has been yet wholly made out. A certain number of the coloured corpuscles undergo disintegration in the liver and spleen; corpuscles in various degrees of degeneration have been observed in the latter organ.

Origin of the White Corpuscles.—The hyaline corpuscles are derived from the lymphocytes which are formed in the lymphatic glands, and enter the blood-stream by the thoracic duct.

The finely granular leucocytes which are the most numerous white corpuscles in the blood originate either in the same way, or by cell division in the blood-stream itself. Most observers consider they arise in the red marrow.

The coarsely granular eosinophile corpuscles, which form about 5 per cent. of the total leucocytes in normal blood, are found in larger numbers in the connective tissue in various parts of the body; they are found in special abundance in red marrow, in which at one time they were supposed to originate. Most look upon each eosinophile corpuscle as a little unicellular gland, and the mass of corpuscles as a migratory glandular tissue.

Chemistry of the Blood-Corpuscles.

The white blood-corpuscles.—Our chemical knowledge of the white corpuscles is small. Their nucleus consists of nuclein, their cell protoplasm yields proteids belonging to the globulin and nucleo-proteid groups. The nucleo-proteid obtained from them is not quite the same thing as fibrin-ferment (*thrombin*); it is probably the zymogen or precursor of the ferment (*prothrombin*); the action of the calcium salts of the plasma in shed blood is to convert prothrombin into thrombin (see p. 414). The protoplasm of these cells often contains small quantities of fat and glycogen.

The red blood-corpuscles.—1000 parts of red corpuscles contain:—

Water		688 parts.
Solids	Organic	303·88 ,,
	Inorganic	8·12 ,,

One hundred parts of the dry organic matter contain—

Proteid	5 to 12 parts.
Hæmoglobin	86 to 94 ,,
Lecithin	1·8 ,,
Cholesterin	0·1 ,,

The proteid present is identical with the nucleo-proteid of white corpuscles. The mineral matter consists chiefly of chlorides of potassium and sodium, and phosphates of calcium and magnesium. In man potassium chloride is more abundant than sodium chloride; this, however, does not hold good for all animals.

Oxygen is contained in combination with the hæmoglobin to form oxyhæmoglobin. The corpuscles also contain a certain amount of carbonic acid.

Hæmoglobin and Oxyhæmoglobin.—The pigment is by far the most abundant and important of the constituents of the red corpuscles. It is a substance which gives the reactions of a proteid, but differs from most other proteids in containing the element iron, and in being readily crystallisable.

It exists in the blood in two conditions: in arterial blood it is combined loosely with oxygen, is of a bright red colour, and is called oxyhæmoglobin; the other condition is the deoxygenated or reduced hæmoglobin (better called simply hæmoglobin). This is found in the blood after asphyxia. It also occurs in all venous blood —that is, blood which is returning to the heart after it has supplied the tissues with oxygen. Venous blood, however, always contains a considerable quantity of oxyhæmoglobin also. Hæmoglobin is the oxygen-carrier of the body, and it may be called a respiratory pigment.*

Crystals of oxyhæmoglobin† may be obtained with readiness from the blood of such animals as the rat, guinea-pig, or dog; with difficulty from other animals, such as man, ape, and most of the common mammals. The following methods are the best:—

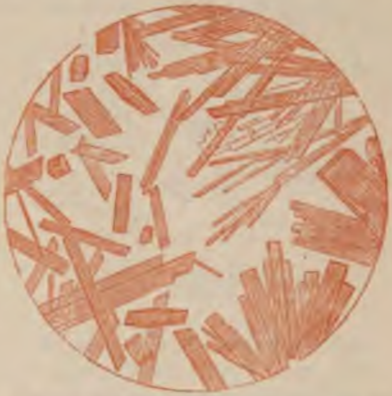


FIG. 362.—Crystals of oxyhæmoglobin—prismatic, from human blood.

1. Mix a drop of defibrinated blood of the rat on a slide with a drop of water; put on a cover-glass; in a few minutes the corpuscles are rendered colourless, and then the oxyhæmoglobin crystallises out from the solution so formed.

2. Microscopical specimens may also be made by Stein's method,

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* In the blood of invertebrate animals hæmoglobin is sometimes found, but usually in the plasma, not in special corpuscles. Sometimes it is replaced by other respiratory pigments, such as the green one, chlorocruorin, found in certain worms, and the blue one, hæmocyanin, found in many molluscs and crustacea. Chlorocruorin contains iron; hæmocyanin contains copper.

† Crystals of hæmoglobin can also be obtained by carrying out the crystallisation in an atmosphere free from oxygen.

which consists in using Canada balsam instead of water in the foregoing experiment.

3. On a larger scale, crystals may be obtained by mixing the blood with one-sixteenth of its volume of ether; the corpuscles dissolve, and the blood assumes a *laky* appearance. After a period varying from a few minutes to days, abundant crystals are deposited.

In nearly all animals the crystals are rhombic prisms (fig. 362); but in the guinea-pig they are rhombic tetrahedra, or four-sided pyramids (fig. 363); in the squirrel and hamster, hexagonal plates (fig. 364).

The crystals contain a varying amount of water of crystallisation; this probably explains their different crystalline form and solubilities. Several observers have analysed hæmoglobin. They find carbon, hydrogen, nitrogen, oxygen, sulphur and iron. The percentage of iron is 0·4. The amounts of the other elements are variously given, but roughly they are the same as in the proteids. On adding an acid or alkali to hæmoglobin, it is broken up into two parts—a brown pigment called *hæmatin*, which contains all the iron of the original substance, and a proteid called *globin*.

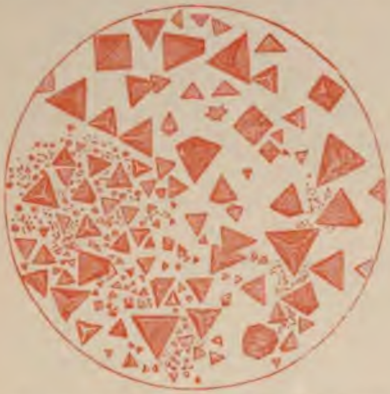

FIG. 363.—Oxyhæmoglobin crystals—tetrahedral, from blood of the guinea-pig.

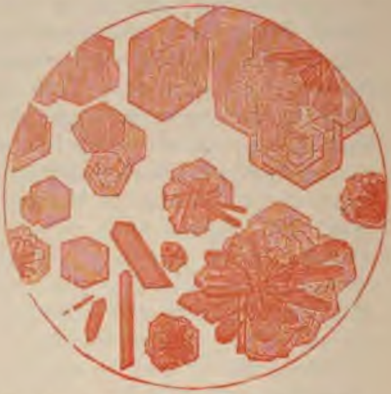

FIG. 364.—Hexagonal oxyhæmoglobin crystals, from blood of squirrel. (After Funke.)

Hæmatin is not crystallisable; it has the formula $C_{34}H_{35}N_4FeO_5$ (Hoppe-Seyler), or $C_{32}H_{30}N_4FeO_3$ (Nencki and Sieber); its constitutional formula is, however, not known. Hæmatin presents different spectroscopic appearances in acid and alkaline solutions (see accompanying plate). On decomposition it yields pyrrol derivatives.

Globin is a somewhat curious proteid; it is coagulable by heat, soluble in dilute acids, and precipitable from such solutions by ammonia. It closely resembles a substance previously separated from red corpuscles by Kossel, and termed by him *histone*. (Schulz.)

Hæmochromogen is sometimes called reduced hæmatin; it may be formed by adding a reducing agent like ammonium sulphide to an alkaline solution of hæmatin. Its absorption spectrum shown on the accompanying plate (No. 8), forms the best spectroscopic test for blood pigment; the suspected pigment is dissolved in potash, and ammonium sulphide added. Very dilute specimens show the absorption bands, especially the one midway between D and E.

Hæmin is of great importance, as the obtaining of this substance forms the best chemical test for blood. Hæmin crystals may be prepared for microscopical examination by boiling a fragment of dried blood with a drop of glacial acetic acid on a slide; on cooling, triclinic plates and prisms of a dark brown colour, often in star-shaped clusters and with rounded angles (fig. 365), separate out. In the case of an old blood stain it is necessary to add a crystal of sodium chloride. Fresh blood contains sufficient sodium chloride in itself.

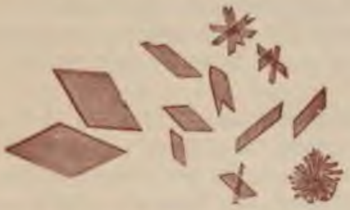
FIG. 365.—Hæmin crystals. (Frey.)

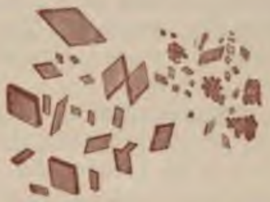
FIG. 366.—Hæmatoidin crystals. (Frey.)

The action of the acetic acid is (1) to split the hæmoglobin into hæmatin and globin; and (2) to evolve hydrochloric acid from the sodium chloride. Hæmin is usually stated to be a combination of hæmatin with hydrochloric acid. Hæmin may be prepared in other ways, but if prepared with the use of acetic acid, Nencki and Zaleski have shown that it also contains an acetyl group, and ascribe to it the empirical formula, $C_{34}H_{33}O_4N_4ClFe$. The chlorine and acetyl are both attached to the iron atom.

Hæmatoporphyrin is iron-free hæmatin; it may be prepared by mixing blood with strong sulphuric acid; the iron is taken out as ferrous sulphate. It is also found sometimes in nature; it occurs in certain invertebrate pigments, and may also be found in certain forms of pathological urine. Even normal urine contains traces of it. It presents different spectroscopic appearances according as it is dissolved in acid or alkaline media. The absorption spectrum figured (No. 9) is that of acid hæmatoporphyrin. (See note, p. 444.)

Hæmatoidin.—This substance is found in the form of yellowish-red crystals (fig. 366) in old blood extravasations, and is derived from the hæmoglobin. Its crystalline form and the reaction it gives with fuming nitric acid shows it to be closely allied to *Bilirubin*, the chief colouring matter of the Bile, and on analysis it is found to be identical with it.

Like hæmatoporphyrin, hæmatoidin is free from iron. These two substances are not identical (*e.g.*, hæmatoidin shows no spectroscopic bands); they are probably isomeric.

Compounds of Hæmoglobin.

Hæmoglobin forms at least four compounds with gases:—

With oxygen	1. Oxyhæmoglobin. 2. Methæmoglobin.
With carbonic oxide	3. Carbonic oxide hæmoglobin.
With nitric oxide	4. Nitric oxide hæmoglobin.

These compounds have similar crystalline forms; they each probably consist of a molecule of hæmoglobin combined with one of the gas in question. They part with the combined gas somewhat readily; they are arranged in order of stability in the above list, the least stable first.

Oxyhæmoglobin is the compound that exists in arterial blood. Many of its properties have been already mentioned. The oxygen linked to the hæmoglobin, which is removed by the tissues through which the blood circulates, may be called the *respiratory oxygen* of hæmoglobin. The processes that occur in the lungs and tissues, resulting in the oxygenation and de-oxygenation respectively of the hæmoglobin, may be imitated outside the body, using either blood or pure solutions of hæmoglobin. The respiratory oxygen can be removed, for example, in the Torricellian vacuum of a mercurial air-pump, or by passing a neutral gas like hydrogen through the blood, or by the use of reducing agents like ammonium sulphide or Stokes' reagent.* One gramme of hæmoglobin will combine with 1·34 c.c. of oxygen.

If any of these methods for reducing oxyhæmoglobin is used, the bright red (arterial) colour of oxyhæmoglobin changes to the purplish (venous) tint of hæmoglobin. On once more allowing oxygen to come into contact with the hæmoglobin, as by shaking the solution with the air, the bright arterial colour returns.

These colour-changes may be more accurately studied with the spectroscope, and the constant position of the absorption bands seen constitutes an important test for blood pigment. It will be first necessary to describe briefly the instrument used.

The Spectroscope.—When a ray of white light is passed through a prism, it is refracted or bent at each surface of the prism; the whole ray is, however, not equally bent, but it is split into its constituent colours, which may be allowed to fall on a screen. The band of colours beginning with the red, passing through orange, yellow, green, blue, and ending with violet, is called a *spectrum:* this is seen in nature in the rainbow. It may be obtained artificially by the glass prism or prisms of a spectroscope.

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* Stokes' reagent must always be freshly prepared; it is a solution of ferrous sulphate to which a little tartaric acid has been added, and then ammonia till the reaction is alkaline.

The spectrum of sunlight is interrupted by numerous dark lines crossing it vertically, called Frauenhofer's lines. These are perfectly constant in position and serve as landmarks in the spectrum. The more prominent are A, B, and C, in the red; D, in the yellow; E, *b*, and F, in the green; G and H, in the violet. These lines are due to certain volatile substances in the solar atmosphere. If the light from burning sodium or its compounds is examined spectroscopically, it will be found to give a bright yellow line, or, rather, two bright yellow lines very close together. Potassium gives two bright red lines and one violet line; and the other elements, when incandescent, give characteristic lines, but none so simple as sodium. If now the flame of a lamp is examined, it will be found to give a continuous spectrum like that of sunlight in the arrangement of its colours, but unlike it in the absence of dark lines; but if the light from the lamp is made to pass through sodium vapour before it reaches the spectroscope, the bright yellow light will be found absent, and in its place a dark line, or, rather, two dark lines very close together, occupying the same position as the two bright lines of the sodium spectrum. The sodium vapour thus absorbs the same rays as those which it itself produces at a higher temperature. Thus the D line, as we term it in the solar spectrum, is due to the presence of sodium vapour in the solar atmosphere. The other dark lines are similarly accounted for by other elements.

The large form of spectroscope (fig. 367) consists of a tube A, called the collimator, with a slit at the end S, and a convex lens at the end L. The latter makes the rays of light passing through the slit from the source of light, parallel: they fall on the prism P, and then the spectrum so formed is focussed by the telescope T.

A third tube, not shown in the figure, carries a small transparent scale of wave-lengths, as in accurate observations the position of any point in the spectrum is given in the terms of the corresponding wave-lengths.

If we now interpose between the source of light and the slit S a piece of coloured glass (H in fig. 367), or a solution of a coloured substance contained in a vessel with parallel sides (the hæmatoscope of Herrmann), the spectrum is found to be no longer continuous, but is interrupted by a number of dark shadows, or *absorption bands* corresponding to the light absorbed by the coloured medium. Thus a solution of oxyhæmoglobin of a certain strength gives two bands between the D and E lines; hæmoglobin gives only one; and other red solutions, though to the naked eye similar to oxyhæmoglobin, will give characteristic bands in other positions.

A convenient form of small spectroscope is the *direct vision spectroscope*, in which, by an arrangement of alternating prisms of crown and flint glass, the spectrum is observed by the eye in the same line as the tube furnished with the slit—indeed, slit and prisms are both contained in the same tube.

In the examination of the spectrum of small coloured objects a combination of the microscope and direct vision spectroscope, called the *micro-spectroscope*, is used.

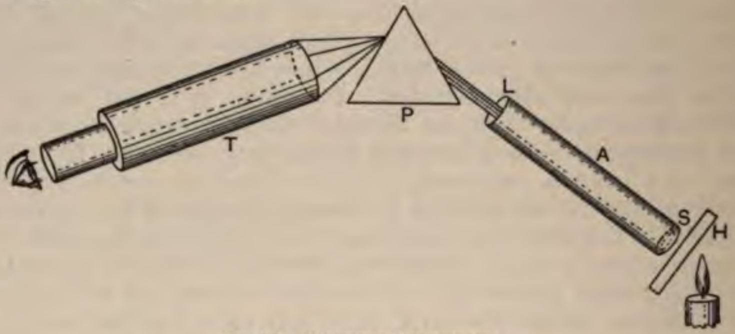
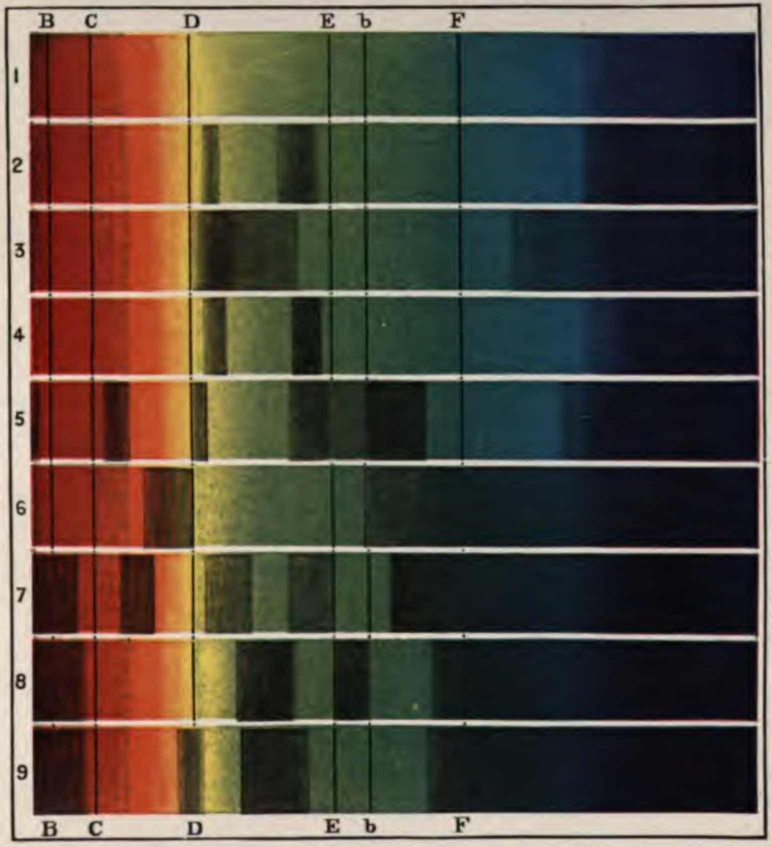


FIG. 367.—Diagram of Spectroscope.

The next figure illustrates a method of representing absorption spectra diagrammatically. The solution was examined in a layer 1 centimetre thick. The base line has on it at the proper distances the chief Frauenhofer lines, and along the right-hand edges are percentages of the amount of oxyhæmoglobin present in I, of hæmoglobin in II. The width of the shadings at each level represents the position and amount of absorption corresponding to the percentages.

The characteristic spectrum of oxyhæmoglobin, as it actually appears through the spectroscope, is seen in the accompanying coloured plate (spectrum 2). There are two distinct absorption bands between the D and E lines; the one nearest to D (the α band) is narrower, darker, and has better-defined edges than the other (the β band). As will be seen on looking at fig. 368, a solution of oxyhæmoglobin of concentration greater than 0·65 per cent. and less than 0·85 per cent. (examined in a cell of the usual thickness of 1 centimetre) gives one thick band overlapping both D and E, and a stronger solution only lets the red light through between C and D. A solution which gives the two characteristic bands must therefore be

BLOOD-SPECTRA COMPARED WITH SOLAR SPECTRUM.



1. Solar spectrum.
2. Spectrum of dilute solution of oxyhæmoglobin.
3. „ „ hæmoglobin.
4. „ „ carbonic oxide hæmoglobin.
5. „ „ acid hæmatin in ethereal solution.
6. „ „ alkaline hæmatin.
7. „ „ methæmoglobin.
8. „ „ hæmochromogen.
9. „ „ acid hæmatoporphyrin.

[*To face page* 434.

a dilute one. The one band (γ band) of hæmoglobin (spectrum 3) is not so well defined as the α or β bands. On dilution it fades rapidly; so that in a solution of such strength that both bands of oxyhæmoglobin would be quite distinct, the single band of hæmoglobin has disappeared from view. The oxyhæmoglobin bands can be distinguished in a solution which contains only one part of the pigment to 10,000 of water, and even in more dilute solutions which seem to be colourless the α band is still visible.

Hæmoglobin and its compounds also show absorption bands in the ultra-violet portion of the spectrum. This portion of the spectrum is not visible to the eye, but can be rendered visible by allowing the spectrum to fall on a fluorescent screen, or on a sensitive photographic plate. In order to show absorption bands in this part of the spectrum very dilute solutions of the pigment must be used.

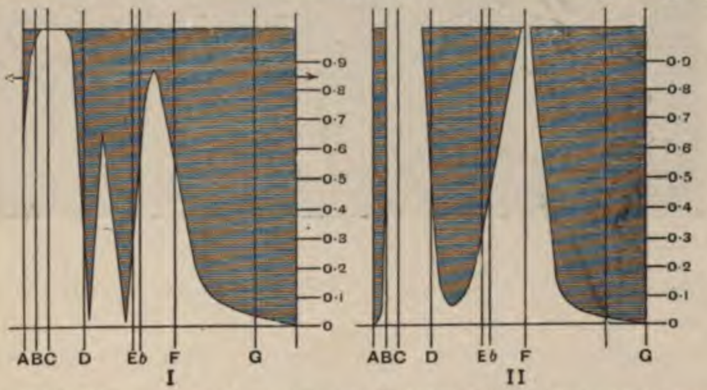


FIG. 368.—Graphic representations of the amount of absorption of light by solution of (I) oxyhæmoglobin, (II) of hæmoglobin, of different strengths. The shading indicates the amount of absorption of the spectrum; the figures on the right border express percentages. (Rollett.)

Oxyhæmoglobin shows a band (Soret's band) between the lines G and H. In hæmoglobin, carbonic oxide hæmoglobin, and nitric oxide hæmoglobin, this band is rather nearer G. Methæmoglobin and hæmatoporphyrin show similar bands.

We owe most of our knowledge of the "photographic spectrum" to Prof. Gamgee, through whose kindness I am enabled to present reproductions of two of his numerous photographs (figs. 369 and 370).

Methæmoglobin.—This may be produced artificially in various ways, as by adding potassium ferricyanide or amyl nitrite to blood, and as it also may occur in certain diseased conditions in the urine, it is of considerable practical importance. It can be crystallised, and is found to contain the same amount of oxygen as oxyhæmoglobin, only combined in a different way. The oxygen is not removable by the air-pump, nor by a stream of neutral gas like hydrogen. It can however, by reducing agents like ammonium sulphide, be made to yield hæmoglobin. Methæmoglobin is of a brownish-red colour, and gives a characteristic absorption band in the red between the C and D lines (spectrum 7 in coloured plate). In dilute solutions other bands can be seen.

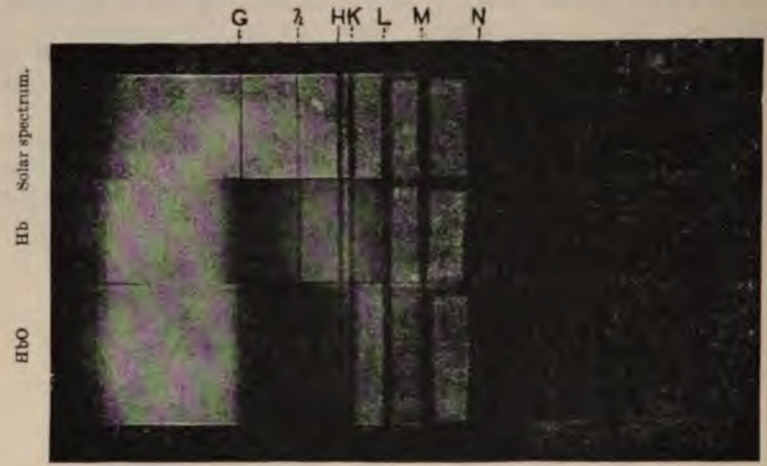


FIG. 369.—The photographic spectrum of hæmoglobin and oxyhæmoglobin. (Gamgee.)

Potassium ferricyanide is the most convenient reagent for making methæmoglobin. It is, however, necessary to mention that it produces another effect as well, namely, it causes an evolution of gas, if the blood has been previously laked by the addition of an equal quantity of water. This gas is oxygen ; in fact, all the

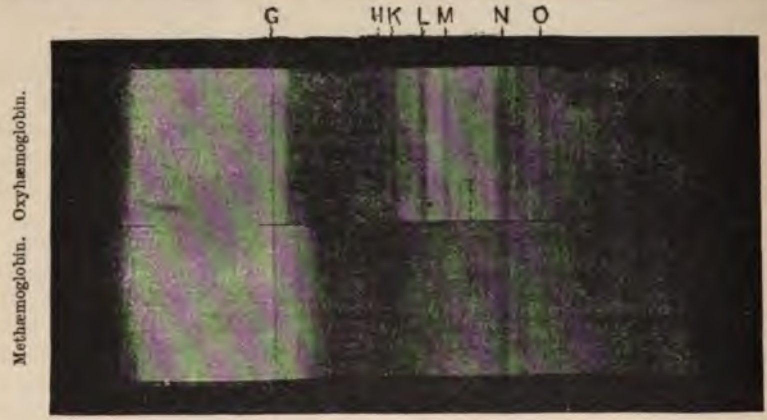


FIG. 370.—The photographic spectrum of oxyhæmoglobin and methæmoglobin. (Gamgee.)

oxygen combined as oxyhæmoglobin is discharged, and this may be collected and measured; the addition of a small amount of sodium carbonate or ammonia to the blood is necessary to prevent the evolution of any carbonic acid. This discharge of oxygen from oxyhæmoglobin is at first sight puzzling, because, as just stated, methæmoglobin contains the same amount of oxygen that is present in oxyhæmoglobin. What occurs is that after the oxygen is discharged from oxyhæmoglobin, an equal quantity of oxygen, due to the oxidising action of the reagents added, takes its place; this new oxygen, however, is combined in some way different from that which was previously united to the hæmoglobin. (Haldane.)

Carbonic oxide hæmoglobin may be readily prepared by passing a stream of carbonic oxide or coal gas through blood or through a solution of oxyhæmoglobin. It has a peculiar cherry-red colour. Its absorption spectrum is very like that of oxyhæmoglobin, but the two bands are slightly nearer the violet end of the spectrum (spectrum 4 in coloured plate). Reducing agents, like ammonium sulphide, do not change it; the gas is more firmly combined than the oxygen in hæmoglobin. CO-hæmoglobin forms crystals like those of oxyhæmoglobin. It resists putrefaction for a very long time.

Carbonic oxide is given off during the imperfect combustion of carbon such as occurs in charcoal stoves or during the explosions that occur in coal-mines; it acts as a powerful poison, by combining with the hæmoglobin of the blood, and thus interferes with normal respiratory processes. The bright colour of the blood in both arteries and veins, and its resistance to reducing-agents, are in such cases characteristic.

Nitric Oxide Hæmoglobin.—When ammonia is added to blood, and then a stream of nitric oxide passed through it, this compound is formed. It may be obtained in crystals isomorphous with oxy- and CO-hæmoglobin. It also has a similar spectrum. It is even more stable than CO-hæmoglobin; it has no practical interest, but is of theoretical importance as completing the series.

Bohr has advanced a theory that hæmoglobin forms a compound with carbonic acid, and that there are numerous oxyhæmoglobins containing different amounts of oxygen, but his views have not been accepted.

Estimation of Hæmoglobin.—The most exact method is by the estimation of the amount of iron (dry hæmoglobin containing ·42 per cent. of iron) in the ash of a given specimen of blood, but as this is a somewhat complicated process, various colorimetric methods have been proposed which, though not so exact, have the advantage of simplicity.

Gowers' Hæmoglobinometer.—The apparatus (fig. 371) consists of two glass tubes of the same size. One contains glycerin jelly tinted with carmine to a standard colour—viz., that of normal blood diluted 100 times with distilled water. The finger is pricked and 20 cubic millimetres of blood are measured out by the capillary pipette, B. This is blown out into the other tube and diluted with distilled water, added drop by drop from the pipette stopper of the bottle, A, until the tint of the diluted blood reaches the standard colour. This tube is graduated into 100 parts. If the tint of the diluted blood is the same as the standard when the tube is filled up to the graduation 100, the quantity of oxyhæmoglobin in the blood is normal. If it has to be diluted more largely, the oxyhæmoglobin is in excess; if to a smaller extent, it is less than normal. If the blood has, for instance, to be diluted up to the graduation 50, the amount of hæmoglobin is only half what it ought to be—50 per cent. of the normal—and so for other percentages.

Haldane's Modification of Gowers' Instrument is the one most frequently used now, and gives very accurate results. Instead of tinted gelatin, the standard of comparison is a sealed tube filled with a solution of carbonic oxide hæmoglobin. This keeps unchanged for years. A stream of coal gas is passed through the blood to be examined. This converts all the hæmoglobin present into carbonic oxide hæmoglobin; this is then diluted with water to match the standard.

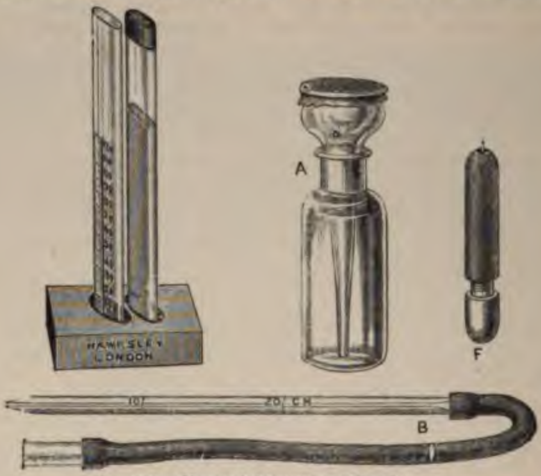


FIG. 371.—Hæmoglobinometer of Dr Gowers.

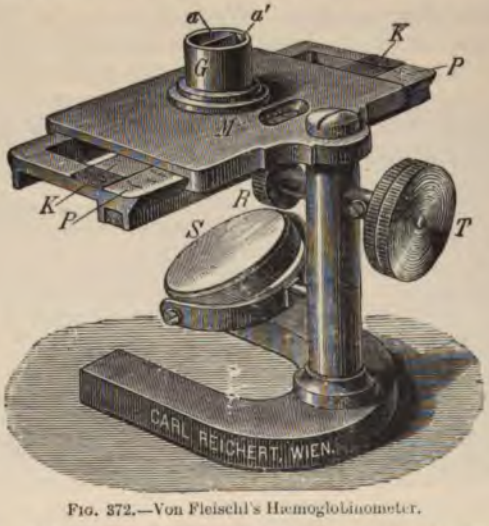


FIG. 372.—Von Fleischl's Hæmoglobinometer.

Von Fleischl's Hæmometer.—The apparatus (fig. 372) consists of a stand bearing a white reflecting surface (S) and a platform. Under the platform is a slot carrying a glass wedge stained red (K) and moved by a wheel (R). On the platform is a small cylindrical vessel divided vertically into two compartments, a and a'.

Fill with a pipette the compartment a' over the wedge with distilled water. Fill about a quarter of the other compartment (a) with distilled water.

Prick the finger and fill the short capillary pipette provided with the instrument with blood. Dissolve this in the water in compartment a, and fill it up with distilled water.

Having arranged the reflector (S) to throw *artificial* light vertically through both compartments, look down through them, and move the wedge of glass by the milled head (T) until the colour of the two is identical. Read off the scale, which is so constructed as to give the percentage of hæmoglobin.

Dr George Oliver's Method consists in comparing a specimen of blood suitably diluted in a shallow white palette with a number of standard tests very carefully prepared by the use of Lovibond's coloured glasses. These standards are much better matches for blood in various degrees of dilution than in most colorimetric methods. The yellow tint of diluted hæmoglobin is very successfully imitated.

Tests for Blood.—These may be gathered from preceding descriptions. Briefly, they are microscopic, spectroscopic, and chemical. The best chemical test is the formation of hæmin crystals. The old test with tincture of guaiacum and hydrogen peroxide, the blood causing the red tincture to become green, is very untrustworthy, as it is also given by many other organic substances.

In medico-legal cases it is often necessary to ascertain whether or not a red fluid or stain upon clothing is or is not blood. In any such case it is advisable not to rely upon one test only, but to try every means of detection at one's disposal. To discover whether it is blood or not is by no means a difficult problem, but to distinguish human blood from that of the common mammals is possible only by the "biological" test described at the end of the next section.

Immunity.

The chemical defences of the body against injury and disease are numerous. The property that the blood possesses of coagulating is a defence against hæmorrhage; the acid of the gastric juice is a great protection against harmful bacteria introduced with food. Bacterial activity in urine is inhibited by the acidity of that secretion.

Far more important and widespread in its effects than any of the foregoing is the bactericidal (*i.e.* bacteria killing) action of the blood and lymph; a study of this question has led to many interesting results especially in connection with the problem of immunity. This subject is one of great importance.

It is a familiar fact that one attack of many infective maladies protects us against another attack of the same disease. The person is said to be *immune* either partially or completely against that disease. Vaccination produces in a patient an attack of cowpox or vaccinia. This disease is either closely related to smallpox, or maybe it is smallpox modified and rendered less malignant by passing through the body of a calf. At any rate, an attack of vaccinia renders a person immune to smallpox, or variola, for a certain number of years. Vaccination is an instance of what is called *protective inoculation*, which is now practised with more or less success in reference to other diseases like plague and typhoid fever. The study of immunity has also rendered possible what may be called *curative inoculation*, or the injection of antitoxic material as a cure for diphtheria, tetanus, snake poisoning, etc.

The power the blood possesses of slaying bacteria was first discovered when the effort was made to grow various kinds of bacteria in it; it was looked upon as probable that blood would prove a suitable soil or medium for this purpose. It was found in some instances to have exactly the opposite effect. The chemical characters of the substances which kill the bacteria are not fully known; indeed, the same is true for most of the substances we have to speak of in this connection. Absence of knowledge on this particular point has not, however, prevented important discoveries from being made.

So far as is known at present, the substances in question are proteid in nature. The bactericidal powers of blood are destroyed by heating it for an hour to 55° C. Whether the substances are enzymes is a disputed point. So also is the question whether they are derived from the leucocytes; the balance of evidence appears to me to be in favour of this view in many cases at any rate, and phagocytosis becomes more intelligible if this view is accepted. The substances, whatever be their source or their chemical nature, are sometimes called alexins, but the more usual name now applied to them is that of *bacterio-lysins*.

Closely allied to the bactericidal power of blood, or blood-serum, is its globulicidal power. By this one means that the blood-serum of one animal has the power of dissolving the red blood-corpuscles of another species. If the serum of one animal is injected into the blood-stream of an animal of another species, the result is a destruction of its red corpuscles, which may be so excessive as to lead to the passing of the liberated hæmoglobin into the urine (hæmoglobinuria). The substance or substances in the serum that possess this property are called *hæmolysins*, and though there is some doubt whether bacterio-lysins and hæmolysins are absolutely identical, there is no doubt that they are closely related substances.

Another interesting chemical point in this connection is the fact that the bactericidal power of the blood is closely related to its alkalinity. Increase of alkalinity means increase of bactericidal power. Venous blood contains more diffusible alkali than arterial blood, and is more bactericidal; dropsical effusions are more alkaline than normal lymph, and kill bacteria more easily. In a condition like diabetes, when the blood is less alkaline than it should be, the susceptibility to infectious diseases is increased. Alkalinity is probably beneficial because it favours those oxidative processes in the cells of the body which are so essential for the maintenance of healthy life.

Normal blood possesses a certain amount of substances which are inimical to the life of our bacterial foes. But suppose a person gets run down; every one knows he is then liable to "catch anything." This coincides with a diminution in the bactericidal power of his blood. But even a perfectly healthy person has not an unlimited supply of bacterio-lysin, and if the bacteria are sufficiently numerous he will fall a victim to the disease they produce. Here, however, comes in the remarkable part of the defence. In the struggle he will produce more and more bacterio-lysin, and if he gets well it means that the bacteria are finally vanquished, and his blood remains rich in the particular bacterio-lysin he has produced, and so will render him immune for a time to further attacks from that particular species of bacterium. Every bacterium seems to cause the development of a specific bacterio-lysin.

Immunity can more conveniently be produced gradually in animals, and this applies, not only to the bacteria, but also to the toxins they form. If, for instance, the bacilli which produce diphtheria are grown in a suitable medium, they produce the diphtheria poison, or toxin, much in the same way that yeast-cells will produce alcohol when grown in a solution of sugar. Diphtheria toxin is associated with a proteose, as is also the case with the poison of snake venom. If a certain small dose called a "lethal dose" is injected into a guinea-pig the result is death. But if the guinea-pig receives a smaller dose it will recover; a few days after it will stand a rather larger dose; and this may be continued until, after many successive gradually increasing doses, it will finally stand an amount equal to many lethal doses without any ill effects. The gradual introduction of the toxin has called forth the production of an antitoxin. If this is done in the horse instead of the guinea-pig the production of antitoxin is still more marked, and the serum obtained from the blood of an immunised horse may be used for injecting into human beings suffering from diphtheria, and rapidly cures the disease. The two actions of the blood, antitoxic and antibacterial, are frequently associated, but may be entirely distinct.

The antitoxin is also a proteid probably of the nature of a globulin; at any rate it is a proteid of larger molecular weight than a proteose. This suggests a practical point. In the case of snake-poisoning the poison gets into the blood rapidly owing to the comparative ease with which it diffuses, and so it is quickly carried all over the body. In treatment with the antitoxin or antivenin, speed is everything if life is to be saved; injection of this material under the skin is not much good, for the diffusion into the blood is too slow. It should be injected straight away into a blood-vessel.

There is no doubt that in these cases the antitoxin neutralises the toxin much in the same way that an acid neutralises an alkali. If the toxin and antitoxin are mixed in a test-tube, and time allowed for the interaction to occur, the result is an innocuous mixture. The toxin, however, is merely neutralised, not destroyed; for if the mixture in the test-tube is heated to 68° C. the antitoxin is coagulated and destroyed and the toxin remains as poisonous as ever.

Immunity is distinguished into *active* and *passive*. Active immunity is produced by the development of protective substances in the body; passive immunity by the injection of a protective serum. Of the two the former is the more permanent.

Ricin, the poisonous proteid of castor-oil seeds, and *abrin*, that of the Jequirity bean, also produce, when gradually given to animals, an immunity, due to the production of antiricin and antiabrin respectively.

Ehrlich's hypothesis to explain such facts is usually spoken of as the *side-chain theory* of immunity. He considers that the toxins are capable of uniting with the protoplasm of living cells by possessing groups of atons like those by which nutritive proteids are united to cells during normal assimilation. He terms these *haptophor* groups, and the groups to which these are attached in the cells he terms *receptor* groups. The introduction of a toxin stimulates an excessive production of receptors, which are finally thrown out into the circulation, and the free circulating receptors constitute the antitoxin. The comparison of the process to assimilation is justified by the fact that non-toxic substances like milk or egg-white introduced gradually by successive doses into the blood-stream cause the formation of anti-substances capable of coagulating them.

Up to this point I have spoken only of the blood, but month by month workers are bringing forward evidence to show that other cells of the body may by similar measures be rendered capable of producing a corresponding protective mechanism.

One further development of the theory I must mention. At least two different substances are necessary to render a serum bactericidal or globulicidal. The bacterio-lysin or hæmolysin consists of these two substances. One of these is called the *immune body*, the other the *complement*. We may illustrate the use of these terms by an example. The repeated injection of the blood of one animal (*e.g.* the goat) into the blood of another animal (*e.g.* a sheep) after a time renders the latter animal immune to further injections, and at the same time causes the production of a serum which dissolves readily the red blood-corpuscles of the first animal. The sheep's serum is thus hæmolytic towards goat's blood-corpuscles. This power is destroyed by heating to 56° C. for half an hour, but returns when the fresh serum of any animal is added. The specific immunising substance formed in the sheep is called the immune body; the ferment-like substance destroyed by heat is the complement. The latter is not specific, since it is furnished by the blood of non-immunised animals, but it is nevertheless essential for hæmolysis. Ehrlich believes that the immune body has two side groups—one which connects with the receptor of the red corpuscles, and one which unites with the haptophor group of the complement, and thus renders possible the ferment-like action of the complement on the red corpuscles. Various antibacterial serums which have not been the success in treating disease they were expected to be, are probably too poor in complement, though they may contain plenty of the immune body.

To put it another way: the cell-dissolving substances cannot act on their objects of attack without an intermediate substance to anchor them on to the substance in question. This intermediary substance, known as the immune body or amboceptor, is specific, and varies with the substance to be attacked (red corpuscles, bacterium, toxin, etc.). The complement may be compared to a person who wants to unlock a door; to do this effectively he must be provided with the proper key (amboceptor or immune body).

Quite distinct from the bactericidal, globulicidal, and antitoxic properties of blood is its agglutinating action. This is another result of infection with many kinds of bacteria or their toxins. The blood acquires the property of rendering immobile and clumping together the specific bacteria used in the infection. The test applied to the blood in cases of typhoid fever, and generally called Widal's reaction, depends on this fact.

The substances that produce this effect are called *agglutinins.* They also are probably proteid-like in nature, but are more resistant to heat than the lysins. Prolonged heating to over 60° C. is necessary to destroy their activity.

Lastly, we come to a question which more directly appeals to the physiologist than the preceding, because experiments in relation to immunity have furnished us with what has hitherto been lacking, a means of distinguishing human blood from the blood of other animals.

The discovery was made by Tchistovitch (1899), and his original experiment was as follows:—Rabbits, dogs, goats, and guinea-pigs were inoculated with eel-serum, which is toxic: he thereby obtained from these animals an antitoxic serum. But the serum was not only antitoxic, but produced a precipitate when added to eel-serum, but not when added to the serum of any other animal. In other words, not only has a specific antitoxin been produced, but also a specific *precipitin*. Numerous observers have since found that this is a general rule throughout the animal kingdom, including man. If, for instance, a rabbit is treated with human blood, the serum ultimately obtained from the rabbit contains a specific precipitin for human blood; that is to say, a precipitate is formed on adding such a rabbit's serum to human blood, but not when added to the blood of any other animal. There may be a slight reaction with the blood of allied animals; for instance, with monkey's blood in the case of man. The great value of the test is its delicacy; it will detect the specific blood when it is greatly diluted, after it has been dried for weeks, or even when it is mixed with the blood of other animals.

We thus see that the means of defence in the body are numerous. In some cases bacteria are killed by the bacteriolysins of the blood; in other cases the toxins the bacteria produce are neutralized by antitoxins. In other cases still the bacteria are directly attacked and devoured by the white corpuscles or phagocytes. In connection with phagocytosis great differences are noticeable; this is partly explained by what is called *chemotaxis;* some bacteria produce chemical substances that attract the leucocytes to their neighbourhood (position chemotaxis): in other cases, such chemical magnets are not produced, or even negative chemotaxis may occur and the phagocytes be repelled. The recent discovery of *opsonins* by A. E. Wright is in this connection one of great importance; it illustrates how the body fluids and the leucocytes co-operate, and further shows how elaborate are the means the body possesses for combating bacterial invasion. The word opsonin is derived from a Greek word which means "to prepare the feast." Washed bacteria from a culture are distasteful to phagocytes; but if the bacteria have been previously soaked in serum, especially if that serum has been obtained from the blood of an animal previously immunised against that special bacterium, then the leucocytes devour them eagerly; in other words, something has been added to the bacterium to make it tasty, and each kind of bacterium apparently requires its own special sauce or opsonin.

Hæmatoporphyrin (see p. 431). If oxyhæmoglobin is treated with dilute acids the result is a formation of hæmatin and globin, but if strong sulphuric acid is employed the iron is removed from the hæmatin and so hæmatoporphyrin is obtained. The stability of the iron in the molecule is due to the presence of oxygen, for with the reduced pigment, hæmatoporphyrin is obtained even when dilute acids are employed. Pure hæmatoporphyrin can once more be converted into hæmatin (that is, the iron can be replaced) by warming a solution in dilute ammonia and adding a little Stokes' fluid, and a few drops of a reducing agent like hydrazine hydrate. If cuprammonium solution is used instead of Stokes' fluid in this experiment, a copper compound of hæmatoporphyrin is obtained, which is identical with *turacin*, the bright red copper-containing pigment found in the plumage of the plantain-eating birds. (Laidlaw.)

CHAPTER XXVII

THE ALIMENTARY CANAL

The alimentary canal consists of a long muscular tube lined by mucous membrane beginning at the mouth, and terminating at the anus. It comprises the mouth, pharynx, œsophagus, stomach, small intestine and large intestine. Opening into it are numerous glands which pour juices into it; these bring about the digestion of the food as it passes along. Some of the glands, like the gastric and intestinal glands, are situated in the lining mucous membrane of the canal; others, like the salivary glands, liver, and pancreas, are situated at a distance from the main canal, and pour their secretion into it by means of side tubes or ducts.

The Mouth

This cavity is lined by a mucous membrane consisting of a *corium* of fibrous tissue with numerous patches of lymphoid tissue in it, especially in the posterior regions; and an epithelium of the stratified variety closely resembling the epidermis. The surface layers, like those of the epidermis, are made of horny scales. Opening into the mouth are a large number of little mucous glands, and the salivary glands pour their secretion into the mouth also. The teeth (p. 64) have been previously studied. The tongue will be considered later in connection with taste.

The Pharynx

That portion of the alimentary canal which intervenes between the mouth and the œsophagus is termed the *Pharynx*. It is constructed of a series of three muscles with striated fibres (*constrictors*), which are covered by a thin fascia externally, and are lined internally by a strong fascia (pharyngeal aponeurosis), on the inner aspect of which is areolar (submucous) tissue and mucous membrane, continuous with that of the mouth, and, as regards the part concerned in swallowing, identical with it in general structure. The epithelium of this part of the pharynx, like that of the mouth, is stratified.

The upper portion of the pharynx into which the nares open is lined with ciliated epithelium.

The pharynx is well supplied with mucous glands.

Between the anterior and posterior arches of the soft palate are situated the *Tonsils*, one on each side. A tonsil consists of an elevation of the mucous membrane presenting 12 to 15 orifices, which lead into crypts or recesses, in the walls of which are placed nodules of lymphoid tissue (fig. 373). These nodules are enveloped in a less dense adenoid tissue which reaches the mucous surface. The surface is covered with stratified epithelium, and the corium may present rudimentary papillæ formed of adenoid tissue. The tonsil is bounded beneath by a fibrous capsule (fig. 373, 4). Into the crypts open the ducts of numerous mucous glands.

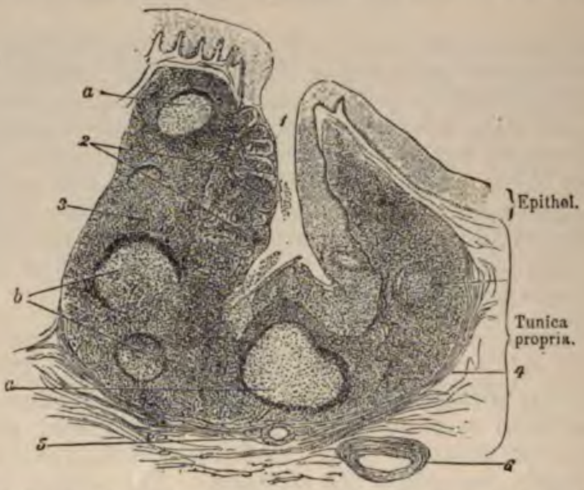


FIG. 373.—Vertical section through a crypt of the human tonsil. 1, entrance to the crypt; 2 and 3, the framework of adenoid tissue; 4, the enclosing fibrous tissue; *a* and *b*, lymphoid nodules; 5 and 6, blood-vessels. (Stöhr.)

THE ŒSOPHAGUS OR GULLET

The Œsophagus or Gullet, the narrowest portion of the alimentary canal, is a muscular tube, nine or ten inches in length, which extends from the lower end of the pharynx to the cardiac orifice of the stomach. It is made up of three coats—viz., the outer, *muscular;* the middle, *submucous;* and the inner, *mucous*. The *muscular* coat is covered externally by a varying amount of loose fibrous tissue. It is composed of two layers of fibres, the outer being arranged longitudinally, and the inner circularly. At the upper part of the œsophagus this coat is made up principally of striated muscle fibres; they are continuous with the constrictor muscles of the pharynx; but lower down the unstriated fibres become more and more numerous, and towards the end of the tube form the entire coat. The muscular coat is connected with the mucous coat by a more or less developed layer of areolar tissue, which forms the *submucous* coat, in which are contained in the lower half or third of the tube many mucous glands, the ducts of which, passing through the mucous membrane, open on its surface (fig. 374). In the deepest part of the mucous membrane is a well-developed layer of longitudinally arranged unstriated muscle, called the *muscularis mucosæ.* The corium of the mucous membrane is composed of fine connective tissue, which, towards the surface, is elevated into papillæ. It is covered with a stratified epithelium, of which the most superficial layers are composed of squamous cells. The epithelium is arranged upon a basement membrane.

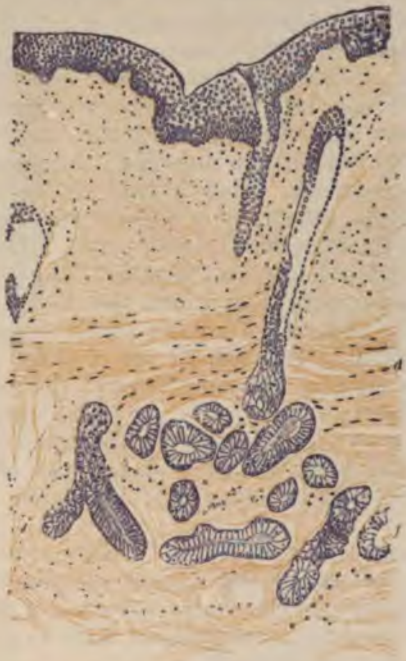


FIG. 374.—Section of the mucous membrane and submucous coat of the œsophagus.

In newly-born children the corium exhibits, in many parts, the structure of lymphoid tissue (Klein).

THE STOMACH

The stomach is a dilatation of the alimentary canal placed between and continuous with the œsophagus, which enters its larger or cardiac end on the one hand, and the small intestine, which commences at its narrowed end or pylorus, on the other.

Its wall is composed of four coats, (1) an external or peritoneal, (2) muscular, (3) submucous, and (4) mucous coat; with blood-vessels, lymphatics, and nerves distributed in and between them.

(1) The *peritoneal* coat has the structure of serous membranes in general. (2) The *muscular* coat consists of three separate layers or sets of fibres, which, according to their several directions, are named the longitudinal, circular, and oblique. The *longitudinal* set are the most superficial: they are continuous with the longitudinal fibres of the œsophagus, and spread out in a diverging manner over the cardiac end and sides of the stomach. They extend as far as the pylorus, being especially distinct at the lesser or upper curvature of the stomach, along which they pass in several strong bands. The next set, the *circular* or *transverse* fibres, are most abundant at the middle and in the pyloric portion of the organ, and form the chief part of the thick projecting ring of the pylorus. They are continuous with the circular layer of the intestine. The deepest set of fibres are the *oblique*, continuous with the circular muscular fibres of the œsophagus: they are comparatively few in number, and are found only at the cardiac portion of the stomach; they form a sphincter around the cardiac orifice. The muscular fibres of the stomach and of the intestinal canal are *unstriated*, being composed of elongated, spindle-shaped fibre-cells.

(3) The *submucous coat* consists of loose areolar tissue, which connects the muscular coat to the mucous membrane. It contains blood-vessels and nerves; in the contracted state of the stomach it is thrown into numerous, chiefly longitudinal, folds or rugæ, which disappear when the organ is distended.

(4) The *mucous membrane* is composed of a corium of fine connective tissue, which approaches closely in structure to adenoid tissue; this tissue supports the tubular glands of which the superficial and chief part of the mucous membrane is composed, and passing up between them assists in binding them together. The glands are separated from the rest of the mucous membrane by a very fine homogeneous basement membrane. The corium is covered with a layer of columnar epithelium, which passes down into the mouths of the glands.

At the deepest part of the mucous membrane are two thin layers (circular and longitudinal) of unstriped muscular fibres, called the *muscularis mucosæ*.

When examined with a lens, the internal or free surface of the stomach presents a peculiar honeycomb appearance, produced by shallow polygonal depressions, the diameter of which varies generally from $\frac{1}{200}$th to $\frac{1}{350}$th of an inch (about 125μ); but near the pylorus is as much as $\frac{1}{100}$th of an inch (250μ). In the bottom of these little pits, and to some extent between them, minute openings are visible, which are the orifices of the ducts of perpendicularly arranged tubular glands (fig. 375), imbedded side by side in sets or bundles, on the surface of the mucous membrane, and composing nearly the whole structure.

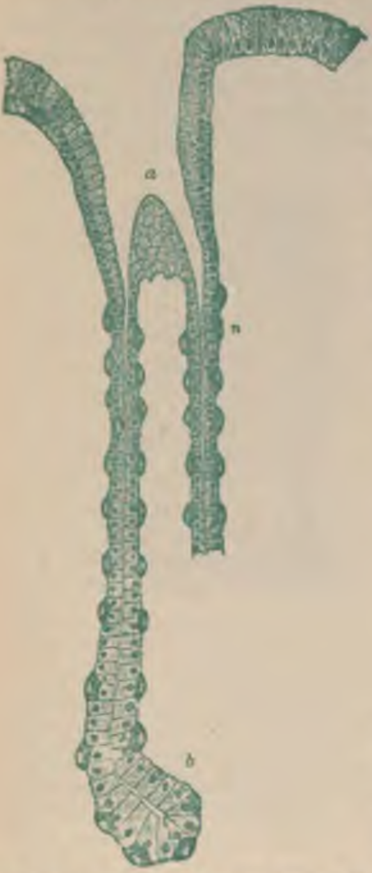


FIG. 375.—From a vertical section through the mucous membrane of the cardiac end of stomach. Two glands are shown with a duct common to both. *a*, duct with columnar epithelium becoming shorter as the cells are traced downward; *n*, neck of gland tubes, with central and parietal cells; *b*, fundus with curved cæcal extremity—the parietal cells are not so numerous here. (Klein and Noble Smith.)

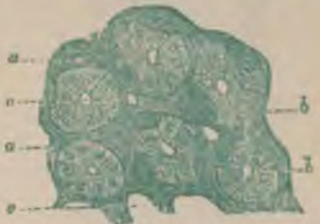


FIG. 376.—Transverse section through lower part of cardiac glands of a cat. *a*, parietal cells; *b*, central cells; *c*, transverse section of capillaries. (Frey.)

The glands of the mucous membrane are of two varieties, (*a*) Cardiac, (*b*) Pyloric.

(*a*) *Cardiac* glands are found throughout the whole of the cardiac half and fundus of the stomach. They are arranged in groups of four or five, which are separated by a fine connective tissue. Two or three tubes open into one duct, which forms about a third of the whole length of the tube and opens on the surface. The ducts are lined with columnar epithelium. Of the gland-tube proper, *i.e.* the part of the gland below the duct, the upper third is the *neck* and the rest the *body*. The neck is narrower than the body, and is lined with coarsely granular polyhedral cells which are continuous with the columnar cells of the duct. Between these cells and the basement membrane of the tubes, are large oval or spherical cells, opaque or granular in appearance, with clear oval nuclei, bulging out the basement membrane; these cells are called *parietal cells.* They do not form a continuous layer. The body which is broader than the neck, and terminates in a blind extremity or *fundus* near the muscularis mucosæ, is lined by cells continuous with the *central* cells of the neck, but longer, more columnar and more transparent. In this part are a few parietal cells of the same kind as in the neck (fig. 375).

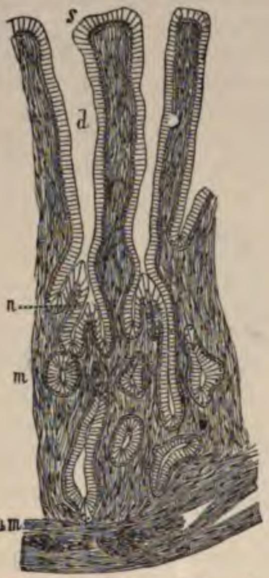


FIG. 377.—Section showing the pyloric glands. *s*, free surface; *d*, ducts of pyloric glands; *n*, neck of same; *m*, the gland tubules; *mm*, muscularis mucosæ. (Klein and Noble Smith.)

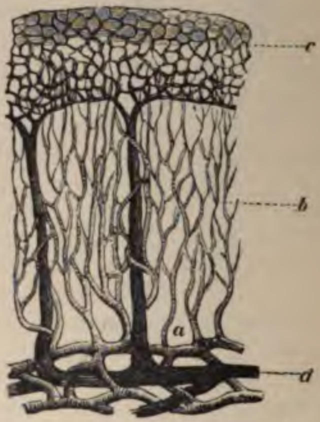


FIG. 378.—Plan of the blood-vessels of the stomach, as they would be seen in a vertical section. *a*, arteries, passing up from the vessels of submucous coat; *b*, capillaries branching between and around the tubes; *c*, superficial plexus of capillaries occupying the ridges of the mucous membrane; *d*, vein formed by the union of veins which, having collected the blood of the superficial capillary plexus, are seen passing down between the tubes. (Brinton.)

(*b*) *Pyloric Glands.*—These glands (fig. 377) have much longer ducts than the cardiac glands. Into each duct two or three tubes open by very short and narrow necks, and the body of each tube is branched, wavy, and convoluted. The lumen is large. The ducts are lined with columnar epithelium, and the neck and body with shorter and finely granular cubical cells, which correspond with the central cells of the cardiac glands. As they approach the duodenum the pyloric glands become larger, more convoluted and more deeply situated. They are directly continuous with Brunner's glands in the duodenum.

Lymphatics.—Lymphatic vessels surround the gland tubes to a greater or less extent. Towards the fundus of the cardiac glands are found masses of lymphoid tissue, which may appear as distinct follicles, somewhat like the solitary glands of the small intestine.

Blood-vessels.—The blood-vessels of the stomach, which first break up in the sub-mucous tissue, send branches upward between the closely packed glandular tubes, anastomosing around them by means of a fine capillary network, with oblong meshes. Continuous with this deeper plexus, or prolonged upwards from it, is a more superficial network of larger capillaries, which branch densely around the orifices of the tubes, and form the framework on which are moulded the small elevated ridges of mucous membrane bounding the minute, polygonal pits before referred to. From this *superficial* network the veins chiefly take their origin. Thence passing down between the tubes, with no very free connection with the deeper *inter-tubular* capillary plexus, they open finally into the venous network in the submucous tissue (fig. 378).

Nerves.—The nerves of the stomach are derived from the pneumogastric and sympathetic, and form two plexuses, one in the submucous and the other between the muscular layers.

These plexuses are continuous with those which occur in the same situations in the intestine, and which we shall again refer to there.

THE INTESTINES.

The Intestinal Canal is divided into two chief portions, named, from their differences in diameter, the *small* and *large* intestine. These are continuous with each other, and communicate by means of an opening guarded by a valve, the *ileo-cæcal* valve, which allows the passage of the products of digestion from the small into the large bowel, but not, under ordinary circumstances, in the opposite direction.

The Small Intestine, the average length of which in an adult is about twenty feet, has been divided, for convenience of description, into three portions, viz., the *duodenum*, which extends for eight or ten inches beyond the pylorus; the *jejunum*, which forms two-fifths, and the *ileum*, which forms three-fifths of the rest of the canal.

Like the stomach, it is constructed of four coats, viz., the serous, muscular, submucous, and mucous.

(1.) The *serous* coat is formed by the visceral layer of the peritoneum, and has the structure of serous membranes in general.

(2.) The *muscular* coat consists of an internal circular and an external longitudinal layer: the former is usually considerably the thicker. Both alike consist of bundles of unstriped muscle supported by connective tissue. They are well provided with lymphatic vessels, which form a set distinct from those of the mucous membrane.

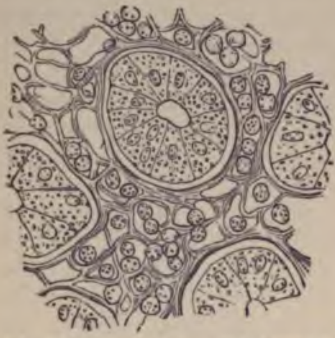


FIG. 379.—Horizontal section of a small fragment of the mucous membrane, including one entire crypt of Lieberkühn and parts of several others. The glands are separated by loose adenoid tissue.

Between the two muscular coats is a nerve-plexus (Auerbach's plexus) (fig. 380), similar in structure to Meissner's (in the submucous coat), but coarser and with more numerous ganglia.

(3) Between the mucous and muscular coats is the *submucous* coat, which consists of connective tissue in which numerous blood-vessels and lymphatics ramify. A fine plexus, consisting mainly of non-medullated nerve-fibres, *Meissner's plexus,* with ganglion cells at its nodes, occurs in the submucous tissue from the stomach to the anus.

(4) The *mucous membrane* is the most important coat in relation to the function of digestion. Its general structure resembles that of the stomach, and, like it, is lined on its inner surface by columnar epithelium. Adenoid tissue (fig. 379) enters largely into its construction; and on its deep surface is the *muscularis mucosæ* (*m,* fig. 382).

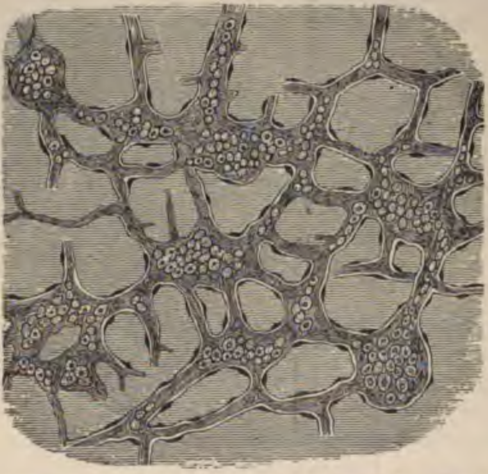


FIG. 380.—Auerbach's nerve-plexus in small intestine. Ganglion-cells are imbedded in the plexus, the whole of which is enclosed in a nucleated sheath. (Klein.)

the fibres of which are arranged in two layers: the outer longitudinal and the inner circular.

Valvulæ Conniventes.—The valvulæ conniventes (fig. 381) commence in the duodenum, about one or two inches beyond the pylorus, and, becoming larger and more numerous immediately beyond the entrance of the bile duct, continue thickly arranged and well developed throughout the jejunum; then, gradually diminishing in size and number, they cease near the middle of the ileum. They are formed by a doubling inwards of the mucous membrane; the crescentic, nearly circular, folds thus formed are arranged transversely to the axis of the intestine, but each individual fold seldom extends around more than $\frac{1}{2}$ or $\frac{2}{3}$ of the bowel's circumference. Unlike the rugæ in the œsophagus and stomach, they do not disappear on distension of the canal. Their function is to afford a largely increased surface for secretion and absorption. They are covered with villi.

Villi.—The Villi (figs. 382, 383, and 384) are confined exclusively to the mucous membrane of the small intestine. They are minute vascular processes, from $\frac{1}{48}$ to $\frac{1}{8}$ of an inch (·5 to 3 mm.) in length, covering the surface of the mucous membrane, and giving it a peculiar velvety, fleecy appearance. Krause estimates them at fifty to ninety in number in a square line at the upper part of the small intestine, and at forty to seventy in the same area at the lower part. They vary in form even in the same animal, and differ according as the lymphatic vessels or *lacteals* which they contain are empty or full; being usually, in the former case, flat and pointed at their summits, in the latter cylindrical.

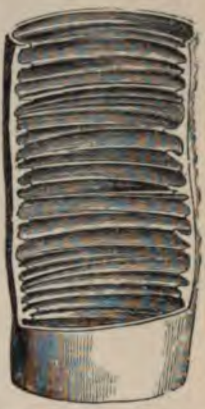


FIG. 381.—Piece of small intestine (previously distended and hardened by alcohol), laid open to show the normal position of the valvulæ conniventes. Natural size.

Each villus consists of a small projection of mucous membrane; its interior consists of fine adenoid tissue, which forms the framework in which the other constituents are contained.

The surface of the villus is clothed by columnar epithelium, which rests on a fine basement membrane; while within this are found, reckoning from without inwards, blood-vessels, fibres of the *muscularis mucosæ*, and a lymphatic or lacteal vessel sometimes looped or branched (fig. 384).

The epithelium is continuous with that lining the other parts of the mucous membrane. The cells are arranged with their long axis radiating from the surface of the villus (fig. 383), and their smaller ends resting on the basement membrane. The free surface of the epithelial cells of the villi, like that of the cells which cover the general surface of the mucous membrane, is surmounted by a bright *striated border* (see pp. 25-27).

Immediately beneath the basement membrane there is a rich supply of *blood-vessels.* Two or more minute arteries are distributed within each villus; and from their capillaries, which form a dense network, proceed one or two small veins, which pass out at the base of the villus.

The layer of the *muscularis mucosæ* in the villus forms a kind of thin hollow cone immediately around the central lacteal, and is, therefore, situated beneath the blood-vessels. It is instrumental in the propulsion of chyle along the lacteal.

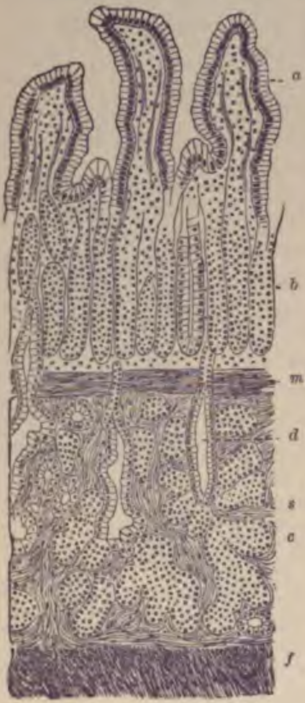


FIG. 382.—Vertical section of duodenum, showing *a*, villi; *b*, crypts of Lieberkühn, and *c*, Brunner's glands in the submucosa *s*, with ducts, *d*; muscularis mucosæ, *m*; and circular muscular coat, *f*. (Schofield.)

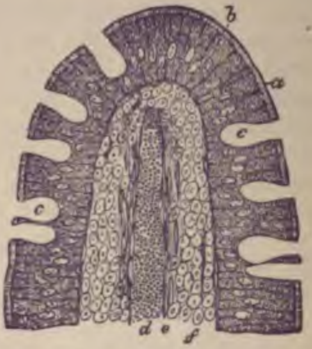


FIG. 383.—Vertical section of a villus of the small intestine of a cat. *a*, striated border of the epithelium; *b*, columnar epithelium; *c*, goblet cells; *d*, central lymph-vessel; *e*, smooth muscular fibres; *f*, adenoid stroma of the villus in which lymph corpuscles lie. (Klein.)

The *lacteal vessels* form the commencement of the intestinal lymphatic system. Each begins almost at the tip of the villus commonly by a dilated extremity. In the larger villi there may be two small lacteal vessels which join, or the lacteals may form a network in the villus (fig. 384).

Glands.—The glands are of two kinds:—viz., those of Lieberkühn and of Brunner. Peyer's patches and the solitary follicles are composed of lymphoid nodules. Though sometimes called glands, they form no external secretion.

The *glands* or *crypts of Lieberkühn* are tubular depressions of the intestinal mucous membrane, thickly distributed over the whole surface both of the large and small intestines. In the small intestine they are visible only with the aid of a lens; and their orifices appear as minute dots scattered between the villi. They are larger in the large intestine, and increase in size the nearer they approach the anal end of the intestinal tube; and in the rectum their orifices may be visible to the naked eye. In length they vary from $\frac{1}{180}$ to $\frac{1}{60}$ of an inch. Each tubule (fig. 386) is constructed of a fine *basement* *membrane*, lined by a layer of columnar epithelium, many of the cells of which are goblet cells.

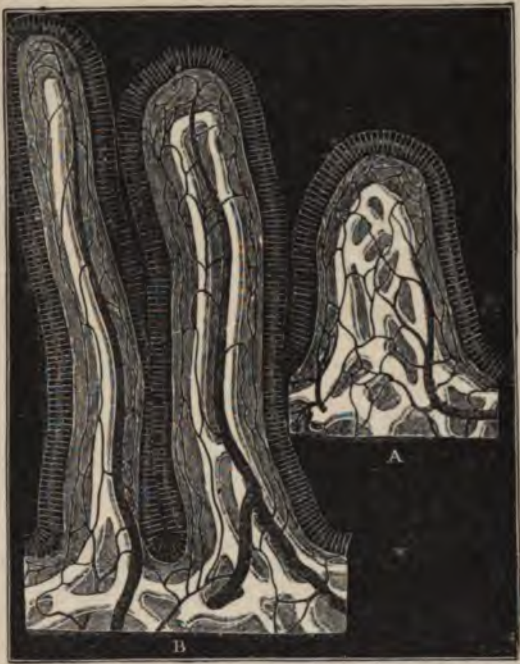


FIG. 384.—A. *Villus of sheep.* B. *Villi of man.* (Slightly altered from Teichmann.)

Brunner's glands (fig. 382) are confined to the duodenum; they are most abundant and thickly set at its commencement, and diminish gradually as the duodenum advances. They are situated beneath the muscularis mucosæ, imbedded in the submucous tissue; each gland is a branched and convoluted tube, lined with columnar epithelium. In structure they are very similar to the pyloric glands of the stomach, but they are more branched and convoluted, and their ducts are longer. The duct of each gland passes through the muscularis mucosæ, and opens on the surface of the mucous membrane.

Peyer's patches are found in greatest abundance in the lower part of the ileum near to the ileo-cæcal valve. They consist of aggregated groups of lymphoid nodules; they vary from one to three inches in length, and are about half-an-inch in width, chiefly of an oval form, their long axes being parallel with that of the intestine. They are almost always placed opposite the attachment of the mesentery.

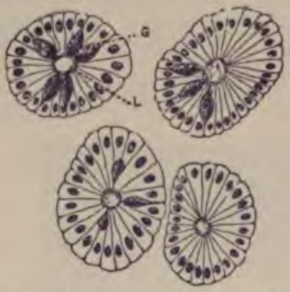


FIG. 385.—Transverse section through four crypts of Lieberkühn from the large intestine of the pig. They are lined by columnar epithelial cells, the nuclei being placed in the outer part of the cells. The divisions between the cells are seen as lines radiating from L, the lumen of the crypt; G, epithelial cells, which have become transformed into goblet cells. × 350. (Klein and Noble Smith.)

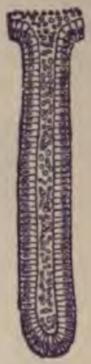


FIG. 386.—A gland of Lieberkühn in longitudinal section. (Brinton.)

When the lymphoid nodules occur singly, as they often do both in small and large intestines, they are called *solitary glands*, or *follicles*.

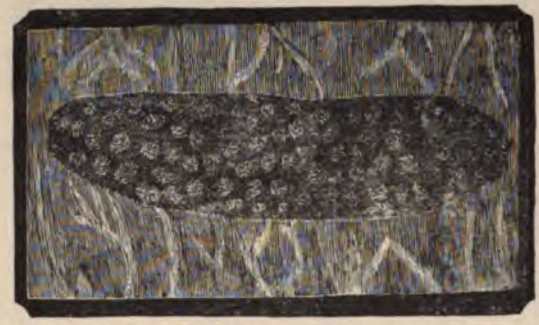


FIG. 387.—Agminate follicles, or Peyer's patch, in a state of distension. × 5. (Boehm.)

The Large Intestine in an adult is from about 4 to 6 feet long; it is subdivided for descriptive purposes into three portions, viz.:—the *cæcum*, a short wide pouch, communicating with the lower end of the small intestine through an opening, guarded by the *ileo-cæcal* valve;

the *colon*, continuous with the cæcum, which forms the principal part of the large intestine, and is divided into ascending, transverse, and descending portions; and the *rectum*, which, after dilating at its lower part, again contracts, and immediately afterwards opens externally through the *anus*. Attached to the cæcum is the small *appendix vermiformis*.

Like the small intestine, the large intestine is constructed of four coats, viz., the serous, muscular, submucous, and mucous. The *serous* coat has connected with it the small processes of peritoneum containing fat, called *appendices epiploicæ*. The fibres of the *muscular* coat, like those of the small intestine, are arranged in two layers—the outer longitudinal, the inner circular. In the cæcum and colon, the longitudinal fibres, instead of being, as in the small intestine, thinly disposed in all parts of the wall of the bowel, are collected, for the most part, into three strong bands, which, being shorter, from end to end, than the other coats of the intestine, hold the canal in folds, bounding intermediate sacculi. On the division of these bands, the intestine can be drawn out to its full length, and it then assumes a uniformly cylindrical form. In the rectum, the fasciculi of these longitudinal bands spread out and mingle with the other longitudinal fibres, forming with them a thicker layer of fibres than exists in any other part of the intestinal canal. The circular muscular fibres are spread over the whole bowel, but are somewhat more marked in the intervals between the sacculi. Towards the lower end of the rectum they become more numerous, and at the anus they form a strong ring called the *internal sphincter* muscle.

The *mucous membrane* of the large, like that of the small intestine, is lined throughout by columnar epithelium, but, unlike it, is quite destitute of villi, and is not projected in the form of *valvulæ conniventes*. It is bounded below by the *muscularis mucosæ*. The arrangement of ganglia and nerve-fibres in the large resembles that in the small intestine.

Glands.—The glands with which the large intestine is provided are simple *tubular* glands, or glands of Lieberkühn; they resemble those of the small intestine, but are somewhat larger and more numerous, and contain a very great number of goblet cells; nodules of *adenoid* or *lymphoid* tissue are most numerous in the cæcum and vermiform appendix. They resemble in shape and structure the solitary glands of the small intestine. Peyer's patches are not found in the large intestine.

Ileo-cæcal Valve.—The ileo-cæcal valve is situated at the place of junction of the small with the large intestine, and guards against any reflux of the contents of the latter into the ileum. It is composed of two semilunar folds of mucous membrane. Each fold is formed by a doubling inwards of the mucous membrane, and is strengthened on the outside by some of the circular muscular fibres of the intestine, which are contained between the outer surfaces of the two layers of which each fold is composed. While the circular muscular fibres, however, at the junction of the ileum with the cæcum are contained between the outer opposed surfaces of the folds of mucous membrane which form the valve, the longitudinal muscular fibres and the peritoneum of the small and large intestine respectively are continuous with each other, without dipping in to follow the circular fibres and the mucous membrane. In this manner, therefore, the folding inwards of these two last-named structures is preserved, while on the other hand, by dividing the longitudinal muscular fibres and the peritoneum, the valve can be made to disappear, just as the constrictions between the sacculi of the large intestine can be made to disappear by performing a similar operation. The mucous membrane of the ileum is continuous with that of the cæcum. That surface of each fold of the ileo-cæcal valve which looks towards the small intestine is covered with villi, while that which looks to the cæcum has none. When the cæcum is distended, the margins of the folds are stretched, and thus are brought into firm apposition one with the other.

CHAPTER XXVIII

FOOD

THE chief chemical compounds or *proximate principles* in food are:—

1. Proteids	organic.
2. Carbohydrates	
3. Fats	
4. Water	inorganic.
5. Salts	

In milk and in eggs, which form the exclusive foods of young animals, all varieties of these proximate principles are present in suitable proportions. Hence they are spoken of as perfect foods. Eggs, though a perfect food for the developing bird, contain too little carbohydrate for a mammal. In most vegetable foods carbohydrates are in excess, while in animal food, like meat, the proteids are predominant. In a suitable diet these should be mixed in proper proportions, which must vary for herbivorous and carnivorous animals.

A healthy and suitable diet must possess the following characters:—

1. It must contain the proper amount and proportion of the various proximate principles.

2. It must be adapted to the climate; to the age of the individual, and to the amount of work done by him.

3. The food must contain not only the necessary amount of proximate principles, but these must be present in a digestible form. As an instance of this, many vegetables (peas, beans, lentils) contain even more proteid than beef or mutton, but are not so nutritious, as they are less digestible, much passing off in the fæces unused.

The nutritive value of a diet depends chiefly on the amount of carbon and nitrogen it contains. A man doing a moderate amount of work will eliminate, chiefly from the lungs, in the form of carbonic acid, from 250 to 280 grammes of carbon *per diem*. During the same time he will eliminate, chiefly in the form of urea in the urine, about

15 to 18 grammes of nitrogen. These substances are derived from the metabolism of the tissues, and various forms of energy, mechanical motion and heat being the chief, are simultaneously liberated. During muscular exercise the output of carbon greatly increases; the increased excretion of nitrogen is not nearly so marked. Taking, then, the state of moderate exercise, it is necessary that the waste of the tissues should be replaced by fresh material in the form of food; and the proportion of carbon to nitrogen should be the same as in the excretions: 250 to 15, or 16·6 to 1. The proportion of carbon to nitrogen in proteid is, however, 53 to 15, or 3·5 to 1. The extra supply of carbon must come from non-nitrogenous food—viz., fat and carbohydrate.

Moleschott gives the following daily diet:—

Proteid	120 grms.
Fat	90 ,,
Carbohydrate	333 ,,

Ranke's diet closely resembles Moleschott's; it is—

Proteid	100 grms.
Fat	100 ,,
Carbohydrate	250 ,,

Such typical diets as these must not be considered as more than rough averages of what is necessary for a man in the course of the day. Actual experience shows that in the diets of different nations there are considerable variations from this standard without the production of ill effects. Age, and the amount of work done, also influence the amount of food necessary; growing children, for instance, require a relatively rich diet; thus, milk, the diet of the infant, is proportionally twice as rich in proteids, and half as rich again in fats, as the normal diet given above. During work more food is necessary than during inactivity.

Some attention has recently been devoted to the question whether as much daily food is necessary as given in the foregoing paragraphs. Hirschfeld showed that for a short time nitrogenous equilibrium can be maintained on a smaller daily supply of nitrogen than 15 grammes. But experiments of others extended over a longer period have shown that sooner or later the body begins to waste if the 15 grammes daily are not supplied. This objection, however, cannot be urged against the experiments of R. O. Neumann, which lasted for three years. The weak point of this research is that it was made only upon one person, namely himself. His diet on the average consisted of 74 grammes of proteid, 117 of fat, and 213 of carbohydrate (equivalent to a total heat value of 2367 large calories, see Chapter XL.). He lost no weight, and part of the time even gained weight; he enjoyed good health, and did his daily duties without inconvenience. A practical point is that his food cost him only 7½d. a day.

There have been other experiments which show that even Europeans can thrive on diets even scantier than this. But to most English people Ranke's and Moleschott's diets would not appear to err on the side of generosity. From the composition of the more commonly used foods taken in fairly average amounts, G. N. Stewart calculates that 500 grammes of bread and 250 grammes of lean meat constitute a fair quantity for a man fit for hard work. Adding 500 grammes of milk, 75 grammes of oatmeal porridge, 30 grammes of butter, and 450 grammes of potatoes, we get, approximately, 20 grammes of nitrogen and 300 grammes of carbon contained in 135 grammes of proteid, 97 grammes of fat, and about 400 grammes of carbohydrate.

Milk.

Milk, which we have already spoken of as a perfect food, is only so for young children. For those who are older, it is so voluminous that unpleasantly large quantities of it would have to be taken in the course of the day to ensure the proper supply of nitrogen and carbon. Moreover, it is relatively too rich in proteid and fat. It also contains too little iron (Bunge): hence children weaned late become anæmic.

The microscope reveals that it consists of two parts: a clear fluid and a number of minute particles that float in it. These consist of minute oil globules, varying in diameter from 0·0015 to 0·005 millimetre (fig. 388).

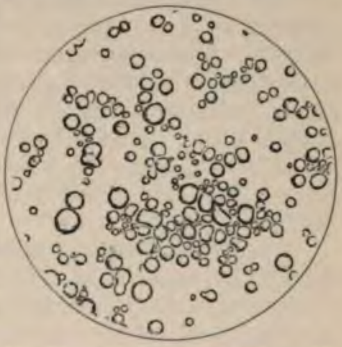


FIG. 388.—Globules of cow's milk. × 400.

The milk secreted during the first few days of lactation is called *colostrum*. It contains very little caseinogen, but large quantities of albumin and globulin instead. It coagulates like white of egg when boiled. Microscopically, cells from the acini of the mammary gland are seen, which contain fat globules in their interior; they are called *colostrum corpuscles.*

Reaction and Specific Gravity.—The reaction of fresh cow's milk and of human milk is amphoteric; that is, it turns blue litmus red, and red litmus blue. This is due to the presence of both acid and alkaline salts. All milk readily turns acid or sour as the result of fermentative change, part of its lactose being transformed into lactic acid. The specific gravity of milk is usually ascertained with the hydrometer. That of normal cow's milk varies from 1028 to 1034. When the milk is skimmed the specific gravity rises, owing to the removal of the light constituent, the fat, to 1033 to 1037. In all cases the specific gravity of water, with which other substances are compared, is taken as 1000.

Composition—Bunge gives the following table, contrasting the milk of woman, and the cow:—

	Woman.	Cow.
	Per cent.	Per cent.
Proteids (chiefly caseinogen)	1·7	3·5
Butter (fat)	3·4	3·7
Lactose	6·2	4·9
Salts	0·2	0·7

Hence, in feeding infants on cow's milk, it is necessary to dilute it, and add sugar to make it approximately equal to natural human milk.

The Proteids of Milk.—The principal proteid in milk is called *caseinogen ;* it is *precipitable* by acids such as acetic acid, and also by saturation with magnesium sulphate, or half saturation with ammonium sulphate, so resembling globulins; it is *coagulated* by rennet to form *casein.* Cheese consists of casein with the entangled fat. The other proteid in milk is an albumin. It is present in small quantities only; it differs in some of its properties (specific rotation, coagulation temperature, and solubilities) from serum-albumin; it is called *lactalbumin.*

The Coagulation of Milk.—Rennet is the agent usually employed for this purpose: it is a ferment secreted by the stomach, especially in sucking animals, and is generally obtained from the calf.

The *curd* consists of the casein and entangled fat: the liquid residue called *whey* contains the sugar, salts, and albumin of the milk. There is also a small quantity of a new proteid called *whey-proteid* which differs from caseinogen by not being convertible into casein; this is produced by the decomposition of the caseinogen molecule during the process of curdling.

The curd formed in human milk is more finely divided than that in cow's milk; and it is more digestible. In feeding children and invalids on cow's milk, the lumpy condition of the curd may be obviated by the addition of lime water or barley water to the milk. There appears to be no chemical difference between the caseinogen of human and that of cow's milk; variations in the amount of calcium salts, and of citric acid account for the differences described.

The addition of rennet produces coagulation in milk, provided that a sufficient amount of calcium salts is present. If the calcium salts are precipitated by the addition of potassium oxalate, rennet causes no formation of casein. The process of curdling in milk is a double one; the first action due to rennet is to produce a change in caseinogen; the second action is that of the calcium salt which precipitates the altered caseinogen as casein. In blood, also, calcium salts are necessary for coagulation, but there they act in a different way, namely, in the production of fibrin ferment (see p. 414).

Caseinogen is not a globulin, though it is, like globulins, readily precipitated by neutral salts. It differs from a globulin in not being coagulated by heat. It is a nucleo-proteid; that is, a compound of a proteid with the proteid-like but phosphorus-rich material called *pseudo-nuclein* (see p. 402). In milk it is combined with calcium to form calcium caseinogenate; when acetic acid is added we therefore get calcium acetate and free caseinogen.

The Fats of Milk.—The chemical composition of the fat of milk (butter) is very like that of adipose tissue. It consists chiefly of palmitin, stearin, and olein. There are, however, smaller quantities of fats derived from fatty acids lower in the series, especially butyrin and caproin. The relation between these varies somewhat, but the proportion is roughly as follows:—Olein, $\frac{3}{7}$; palmitin, $\frac{1}{3}$; stearin, $\frac{1}{6}$; butyrin, caproin, and caprylin, $\frac{1}{14}$. The old statement that each fat globule is surrounded by a film of caseinogen is, according to Ramsden's recent observations, correct. Milk also contains small quantities of lecithin, a phosphorised fat; of cholesterin, an alcohol which resembles fat in its solubilities, and a yellow fatty pigment or lipochrome.

Milk Sugar, or Lactose.—This is a saccharose ($C_{12}H_{22}O_{11}$). Its properties have already been described in Chap. XXV., p. 390.

Souring of Milk.—When milk is allowed to stand the chief change which it is apt to undergo is a conversion of a part of its lactose into lactic acid. This is due to the action of micro-organisms, and would not occur if the milk were contained in closed sterilised vessels. Equations showing the change produced are given on p. 391. When souring occurs, the acid formed precipitates a portion of the caseinogen. This must not be confounded with the formation of casein from caseinogen which is produced by rennet. There are, however, some bacteria which, like rennet, produce true coagulation.

Alcoholic Fermentation in Milk.—When yeast is added to milk, the sugar does not readily undergo the alcoholic fermentation. Other somewhat similar fungoid growths are, however, able to produce the change, as in the preparation of koumiss; the milk sugar is first inverted, that is dextrose and galactose are formed from it (see p. 391), and it is these sugars from which alcohol and carbonic acid originate.

The Salts of Milk.—The chief salt present is calcium phosphate; a small quantity of magnesium phosphate is also present. The other salts are chiefly chlorides of sodium and potassium.

The Mammary Glands.

The mammary glands are composed of large divisions or lobes, and these are again divisible into lobules; the lobules are composed of the convoluted and dilated subdivisions of the main ducts held together by connective-tissue. Covering the general surface of the gland, with the exception of the nipple, is a considerable quantity of fat, itself lobulated by sheaths and processes of areolar tissue (fig. 389) connected both with the skin in front and the gland behind; the same bond of connection extends also from the under surface of the gland to the sheathing connective-tissue of the great pectoral muscle on which it lies. The main ducts of the gland, fifteen to twenty in number, called the *lactiferous* ducts, are formed by the union of the smaller (lobular) ducts, and open by small separate orifices through the nipple. At the points of junction of lobular ducts to form lactiferous ducts, and just before these enter the base of the nipple, the ducts are dilated; and during the period of active secretion by the gland, the dilatations form reservoirs for the milk, which collects in and distends them. The walls of the gland-ducts are formed of areolar with some unstriped muscular tissue, and are lined internally by short columnar and near the nipple by flattened epithelium. The alveoli consist of a basement membrane of flattened cells lined by low columnar epithelium (fig. 390).

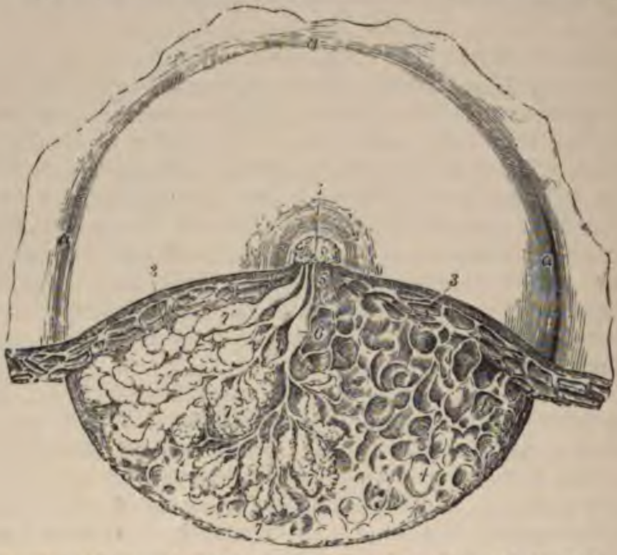


FIG. 389.—Dissection of the lower half of the female mamma, during the period of lactation. $\frac{2}{3}$.—In the left-hand side of the dissected part the glandular lobes are exposed and partially unravelled; and on the right-hand side, the glandular substance has been removed to show the reticular loculi of the connective-tissue in which the glandular lobules are placed: 1, upper part of the mamilla or nipple; 2, areola; 3, subcutaneous masses of fat; 4, reticular loculi of the connective-tissue which support the glandular substance and contain the fatty masses; 5, one of three lactiferous ducts shown passing towards the mamilla where they open; 6, one of the sinus lactei or reservoirs; 7, some of the glandular lobules which have been unravelled; 7', others massed together. (Luschka.)

The nipple is composed of areolar tissue, and contains unstriped muscular fibres. Blood-vessels are also freely supplied to it, so as to give it an erectile structure. On its surface are very sensitive papillæ; and around it is a small area or *areola* of pink or dark-tinted skin, on which are to be seen small projections formed by minute secreting glands.

Blood-vessels, nerves, and lymphatics are plentifully supplied to the mammary glands; the calibre of the blood-vessels, as well as the size of the glands, varies very greatly under certain conditions, especially those of pregnancy and lactation. The secretory nerves of the mammary glands have not yet been discovered.

The alveoli of the glands during the secreting periods are found to be lined with very short columnar cells, with nuclei situated towards the centre. The edges of the cells towards the lumen may be irregular and jagged, and the remainder of the alveolus is filled up with the materials of the milk. During the intervals between the acts of discharge, the cells of the alveoli elongate towards the lumen, their nuclei divide, and in the part of the cells towards the lumen a collection of oil globules and of other materials takes place.

The next stage is that the cells divide and the part of each towards the lumen containing a nucleus and the materials of the secretion, disintegrates and goes to form the solid part of the milk. The cells also secrete water, salts, and milk sugar. The fat, etc., of milk are not simply picked out from the blood by the secreting cells, but these materials are formed by metabolic processes within the protoplasm of the cells.

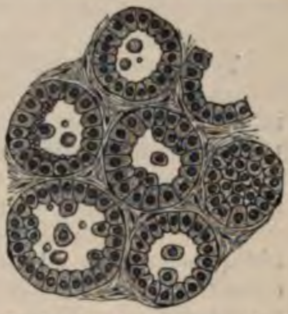


FIG. 390.—Section of mammary gland of bitch, showing acini, lined with epithelial cells of a short columnar form. × 200. (V. D. Harris.)

In the earlier days of lactation, epithelial cells only partially transformed are discharged in the secretion; these are termed *colostrum corpuscles*. It is stated that colostrum possesses a purgative action.

During pregnancy the mammary glands undergo changes (*evolution*) which are readily observable. They enlarge, become harder, and more distinctly lobulated; the veins on the surface become more prominent. The areola becomes enlarged and dusky, with projecting papillæ; the nipple, too, becomes more prominent, and milk can be squeezed from the orifices of the ducts. This is a very gradual process, which commences about the time of conception, and progresses steadily during the whole period of gestation. In the gland itself solid columns of cells bud off from the old alveoli to form new alveoli. But these solid columns after a while are converted into tubes by the central cells becoming fatty and being discharged as the colostrum corpuscles above mentioned.

After the end of lactation, the mamma gradually returns to its original size (*involution*). The acini, in the early stages of involution, are lined with cells in all degrees of vacuolation. As involution proceeds, the acini diminish considerably in size, and at length, instead of a mosaic of lining epithelial cells (twenty to thirty in each acinus), we have five or six nuclei (some with no surrounding protoplasm) lying in an irregular heap within the acinus. During the later stages of involution, large yellow granular cells are to be seen. As the acini diminish in size, the connective-tissue and fatty matter between them increase, and in some animals, when the gland is completely inactive it is found to consist of a thin film of glandular tissue overlying a thick cushion of fat. Many of the products of waste are carried off by the lymphatics.

Eggs.

In this country the eggs of hens and ducks are those particularly selected as foods. The chief constituent of the *shell* is calcium carbonate. The *white* is composed of a richly albuminous fluid enclosed in a network of firmer and more fibrous material. The amount of solids is 13·3 per cent.; of this 12·2 is proteid in nature (egg-albumin, with smaller quantities of egg-globulin, and of a mucinoid substance called ovo-mucoid), and the remainder is made up of sugar (0·5 per cent.), traces of fats, lecithin and cholesterin, and 0·6 per cent. of inorganic salts. The *yolk* is rich in food materials for the development of the future embryo. In it there are two varieties of yolk-spherules, one kind yellow and opaque (due to admixture with fat and a yellow lipochrome), and the other smaller, transparent and almost colourless; these are proteid in nature, consisting of the nucleo-proteid called *vitellin*. Small quantities of sugar, lecithin, cholesterin and inorganic salts are also present.

The nutritive value of eggs is high, as they are so readily digestible; but the more an egg is cooked the more insoluble do its proteid constituents become.

Meat.

This is composed of the muscular and connective (including adipose) tissues of certain animals. The flesh of some animals is not eaten; in some cases this is a matter of fashion, in others, owing to an unpleasant taste, such as the flesh of carnivora is said to have; and in other cases (*e.g.* the horse) because it is more lucrative to use the animal as a beast of burden.

Meat is the most concentrated and most easily assimilable of nitrogenous foods. It is our chief source of nitrogen. Its chief solid constituent is proteid, and the principal proteid is myosin. In addition to the extractives and salts contained in muscle, there is always a certain percentage of fat, even though all visible adipose tissue is dissected off. The fat-cells are placed between the muscular fibres, and the amount of fat so situated varies in different animals; it is particularly abundant in pork; hence the indigestibility of this form of flesh: the fat prevents the gastric juice from obtaining ready access to the muscular fibres.

The following table gives the chief substances in some of the principal meats used as food:—

Constituents.	Ox.	Calf.	Pig.	Horse.	Fowl.	Pike.
Water . . .	76·7	75·6	72·6	74·3	70·8	79·3
Solids . . .	23·3	24·4	27·4	25·7	29·2	20·7
Proteids and gelatin*	20·0	19·4	19·9	21·6	22·7	18·3
Fat	1·5	2·9	6·2	2·5	4·1	0·7
Carbohydrate . .	0·6	0·8	0·6	0·6	1·3	0·9
Salts . . .	1·2	1·3	1·1	1·0	1·1	0·8

The large percentage of water in meat should be particularly noted; if a man wished to take his daily supply of 100 grammes of proteid entirely in the form of meat, it would be necessary for him to consume about 500 grammes (*i.e.*, a little more than 1 lb.) of meat.

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* The flesh of young animals is richer in gelatin than that of old; thus 1000 parts of beef yield 6, of veal 50, parts of gelatin.

Flour.

The best wheat flour is made from the interior of wheat grains, and contains the greater proportion of the starch of the grain and most of the proteid. Whole flour is made from the whole grain *minus* the husk, and thus contains not only the white interior but also the harder and browner outer portion of the grain. This outer region contains a somewhat larger proportion of the proteids of the grain. Whole flour contains 1 to 2 per cent. more proteid than the best white flour, but it has the disadvantage of being less readily digested. Brown flour contains a certain amount of bran in addition; it is still less digestible, but is useful as a mild laxative, the insoluble cellulose mechanically irritating the intestinal canal as it passes along.

The best flour contains very little sugar. The presence of sugar indicates that germination has commenced in the grains. In the manufacture of malt from barley this is purposely allowed to go on.

When mixed with water, wheat flour forms a sticky, adhesive mass called dough. This is due to the formation of gluten, and the forms of grain poor in gluten cannot be made into dough (oats, rice, etc.). Gluten does not exist in the flour as such, but is formed on the addition of water from the pre-existing globulins in the flour.

The following table contrasts the composition of some of the more important vegetable foods:—

Constituents.	Wheat.	Barley.	Oats.	Rice.	Lentils.	Peas.	Potatoes.
Water . .	13·6	13·8	12·4	13·1	12·5	14·8	76·0
Proteid .	12·4	11·1	10·4	7·9	24·8	23·7	2·0
Fat . .	1·4	2·2	5·2	0·9	1·9	1·6	0·2
Starch .	67·9	64·9	57·8	76·5	54·8	49·3	20·6
Cellulose .	2·5	5·3	11·2	0·6	3·6	7·5	0·7
Mineral salts	1·8	2·7	3·0	1·0	2·4	3·1	1·0

We see from this table—

1. The great quantity of starch always present.

2. The small quantity of fat; that bread is generally eaten with butter is a popular recognition of this fact.

3. Proteid, except in potatoes, is pretty abundant, and especially so in the pulses (lentils, peas, etc.). The proteid in the pulses is not gluten, but consists of vitellin and globulin-like substances.

In the mineral matters in vegetables, salts of potassium and magnesium are, as a rule, more abundant than those of sodium and calcium.

Bread.

Bread is made by cooking the dough of wheat flour mixed with yeast, salt, and flavouring materials. A ferment in the flour acts at the commencement of the process, when the temperature is kept a little over that of the body, and forms dextrin and sugar from the starch, and then the alcoholic fermentation, due to the action of the yeast, begins. The bubbles of carbonic acid, burrowing passages through the bread, make it light and spongy. This enables the digestive juices subsequently to soak into it readily and affect all parts of it. In the later stages, viz., baking, the temperature is raised, the gas and alcohol are expelled from the bread, the yeast is killed, and a crust forms from the drying of the outer portions of the dough.

White bread contains, in 100 parts, 7 to 10 of proteid, 55 of carbohydrates, 1 of fat, 2 of salts, and the rest water.

Cooking of Food.

The cooking of foods is a development of civilisation and serves many useful ends:—

1. It destroys all parasites and danger of infection. This relates not only to bacterial growths, but also to larger parasites, such as tapeworms and trichinæ.

2. In the case of vegetable foods it breaks up the starch grains, bursting the cellulose and allowing the digestive juices to come into contact with the granulose.

3. In the case of animal foods it converts the insoluble collagen of the universally distributed connective tissues into the soluble gelatin. The loosening of the fibres is assisted by the formation of steam between them. By thus loosening the binding material, the more important elements of the food, such as muscular fibres, are rendered accessible to the gastric and other juices. Meat before it is cooked is generally kept a certain length of time to allow *rigor mortis* to pass off.

Of the two chief methods of cooking, roasting and boiling, the former is the more economical, as by its means the meat is first surrounded with a coat of coagulated proteid on its exterior, which keeps in the juices to a great extent, letting little else escape but the dripping (fat). Whereas in boiling, unless both bouillon and bouilli are used, there is considerable waste. Cooking, especially boiling, renders the proteids more insoluble than they are in the raw state; but this is counterbalanced by the other advantages that cooking possesses.

In making *beef tea* and similar extracts of meat it is necessary that the meat should be placed in cold water, and this is gradually and carefully warmed. In boiling a joint it is usual to put the meat into boiling water at once, so that the outer part is coagulated, and the loss of material minimised.

An extremely important point in this connection is that beef tea and similar meat extracts should not be regarded as foods. They are valuable as pleasant stimulating drinks for invalids, but they contain very little of the nutritive material of the meat, their chief constituents, next to water, being the salts and extractives of flesh.

Soup contains the extractives of meat, a small proportion of the proteids, and the principal part of the gelatin. The gelatin is usually increased by adding bones and fibrous tissue to the stock. It is the presence of this substance which causes soup when cold to gelatinise.

Accessories to Food.

Among these must be placed *alcohol*, the value of which within moderate limits is not as a food but as a stimulant; *condiments* (mustard, pepper, ginger, curry powder, etc.), which are stomachic stimulants, the abuse of which is followed by dyspeptic troubles; and *tea*, *coffee*, *cocoa*, and similar drinks. These are stimulants chiefly to the nervous system; tea, coffee, maté (Paraguay), guarana (Brazil), cola nut (Central Africa), bush tea (South Africa), and a few other plants used in various countries all owe their chief property to an alkaloid called *theine* or *caffeine* ($C_8H_{10}N_4O_2$); cocoa to the closely related alkaloid, *theobromine* ($C_7H_8N_4O_2$); coca to *cocaine*. These alkaloids are all poisonous, and used in excess, even in the form of infusions of tea and coffee, produce over-excitement, loss of digestive power, and other disorders well known to physicians. Coffee differs from tea in being rich in aromatic matters; tea contains a bitter principle, tannin; to avoid the injurious solution of too much tannin, tea should only be allowed to infuse (draw) for a few minutes. Cocoa is not only a stimulant, but a food in addition; it contains about 50 per cent. of fat, and 12 per cent. of proteid. In manufactured cocoa, the amount of fat is reduced to 30 per cent., and the amount of proteid rises proportionately to about 20 per cent. The quantity of cocoa usually consumed is too small for these food materials to count very much in the daily supply. The amount of proteid in solution (mainly albumose) in a breakfast cup of cocoa is under half a gramme; most of the food stuffs are in suspension, for cocoa is drunk "thick," not as a clear infusion.

Green vegetables are taken as a palatable adjunct to other foods, rather than for their nutritive properties. Their potassium salts are, however, abundant. Cabbage, turnips, and asparagus contain 80 to 92 water, 1 to 2 proteid, 2 to 4 carbohydrates, and 1 to 1·5 cellulose per cent. The small amount of nutriment in most green foods accounts for the large meals made by, and the vast capacity of the alimentary canal of, herbivorous animals.

CHAPTER XXIX

SECRETING GLANDS

BEFORE passing on to the action of the digestive secretions on foods, it will be well to discuss the varieties of glands by means of which these substances are formed.

It is the function of gland-cells to produce by the metabolism of their protoplasm certain substances called secretions. These materials are of two kinds; viz., those which are employed for the purpose of serving some ulterior office in the economy, and those which are discharged from the body as useless or injurious. In the former case the separated materials are termed *secretions;* in the latter they are termed *excretions.*

The secretions, as a rule, consist of substances which do not pre-exist in the same form in the blood, but require special cells and a process of elaboration for their formation, *e.g.*, the liver cells for the formation of bile, the mammary gland-cells for the formation of milk. The excretions, on the other hand, commonly consist of substances which exist ready-formed in the blood, and are merely abstracted therefrom. If from any cause, such as extensive disease or extirpation of an excretory organ, the separation of an excretion is prevented, and an accumulation of it in the blood ensues, it frequently escapes through other organs, and may be detected in various fluids of the body. An instance of this is seen after the kidneys have been removed. Urea then accumulates in the blood. But this is never the case with secretions; for, after the removal of the special organ by which each of them is manufactured, the secretion is no longer formed.

The circumstances of their formation, and their final destination, are, however, the only particulars in which secretions and excretions can be distinguished; for, in general, the structure of the parts engaged in eliminating excretions is as complex as that of the parts concerned in the formation of secretions. It will, therefore, be sufficient to speak in general terms of the process.

Every secreting apparatus consists essentially of a layer of secreting cells arranged round a central cavity; they take from the lymph which bathes them the necessary material, and transform it into the secretion which they pour at high pressure into the cavity.

The principal secreting organs are the following:—(1) the serous and synovial membranes; (2) the mucous membranes with their special glands, *e.g.*, the buccal, gastric and intestinal glands; (3) the salivary glands and pancreas; (4) the mammary glands; (5) the liver; (6) the lacrimal gland; (7) the kidney and skin; and (8) the testes.

Serous membranes.—We have already discussed the structure of *serous* membranes (p. 206), and also the question whether the lymph is a true secretion (pp. 318-320).

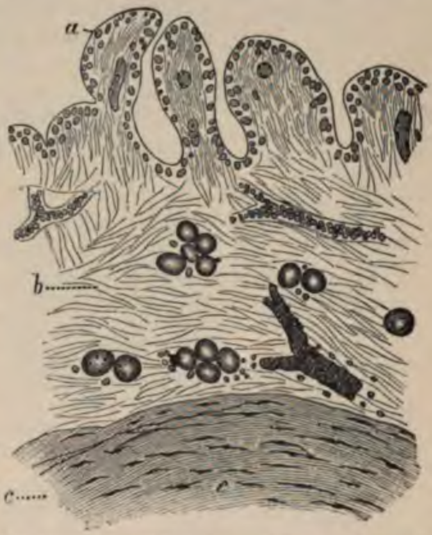

FIG. 391.—Section of synovial membrane. *a*, epithelial covering of the elevations of the membrane; *b*, underlying tissue containing fat and blood-vessels; *c*, ligament covered by the synovial membrane. (Cadiat.)

The synovial membranes line the joints and the sheaths of tendons and ligaments with which we may include the synovial *bursæ*. The contents of these sacs is called *synovia;* it lubricates the surfaces of the joint, and so ensures an easy movement. Synovia is a rich lymph *plus* a mucinoid material; and it is this latter constituent which gives the secretion its viscidity. It is thus a true secretion; and is formed by the epithelial cells which form an imperfect lining to the sac, and which are especially accumulated on the processes of the synovial fringes (fig. 391).

A mucous membrane consists of two parts: the *epithelium* on its surface, and the *corium* of connective tissue beneath. The epithelium generally rests on a basement membrane which is usually composed of clear flattened cells placed edge to edge.

The name *mucous* is derived from the fact that these membranes all secrete *mucin*, the chief constituent of *mucus;* this may be formed from the surface epithelium cells breaking down into goblet cells (see p. 26), or an analogous process may occur in the cells of little glands called mucous glands, situated more or less deeply under the epithelium, and opening on the surface by ducts. Many mucous membranes (*e.g.*, that of the stomach) form other secretions as well.

Mucous membranes line all those passages by which internal parts communicate with the exterior. The principal tracts are the *Digestive*, *Respiratory*, and *Genito-urinary*.

Secreting glands may be classified according to certain types, which are the following:—1. The *simple tubular* gland (A, fig. 392), examples of which are furnished by the crypts of Lieberkühn in the intestinal wall. To the same class may be referred the elongated and tortuous *sudoriferous glands*.

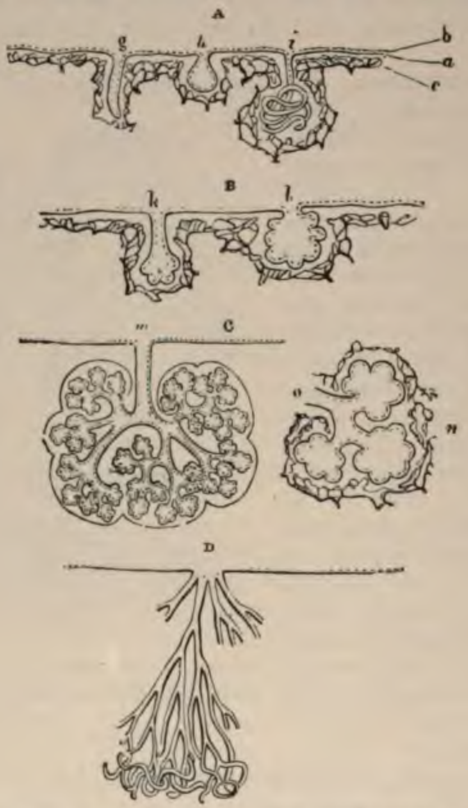

FIG. 392.—Diagram of types of secreting glands. A, simple glands, viz., *g*, straight tube; *h*, sac; *i*, coiled tube. B, multilocular crypts; *k*, of tubular form; *l*, saccular. C, racemose, or saccular compound gland; *m*, entire gland, showing branched duct and lobular structure; *n*, a lobule, detached with *o*, branch of duct proceeding from it. D, compound tubular gland. (Sharpey.)

2. The *compound tubular* glands (D, fig. 392) form another division. These consist of main gland-tubes, which divide and sub-divide.

3. The *racemose* glands are those in which a number of vesicles or *acini* are arranged in groups or lobules (C, fig. 392). The *Meibo-*

mian follicles are examples of this kind of gland. Some glands, like the pancreas, are of a mixed character, combining some of the characters of the tubular with others of the racemose type; these are called *tubulo-racemose* or *tubulo-acinous* glands. These glands differ from each other only in secondary points of structure, but all have the same essential character in consisting of rounded groups of vesicles containing gland-cells, and opening by a common central cavity into minute ducts, which ducts in the large glands converge and unite to form larger and larger tubes, and at length open by one common trunk on a free surface. The larger racemose glands, like the salivary glands, are called *compound racemose* glands.

On internal secretions, see p. 328.

Electrical Variations in Glands.

These have been studied in many glandular organs, but especially in the salivary glands and skin.

In the submaxillary gland the hilus is electro-negative to the external surface of the organ; a current therefore passes from hilus to surface through the galvanometer. If the chorda tympani is stimulated by rapidly interrupted shocks, the surface becomes still more positive. This is the opposite to what occurs in a muscle; there the current of action is in the reverse direction to the demarcation current; the change in the gland is a positive variation in the arithmetical sense. This is abolished by a small dose of atropine; stimulation then causes a small negative variation which is abolished by a larger dose of atropine.

If, before atropine is given, slowly interrupted shocks are used, or rapidly interrupted shocks too weak to excite secretion are employed, the electrical response of the organ is a negative variation. The same is true for stimulation of the sympathetic. Single induction shocks applied to the chorda tympani cause a diphasic variation, first the surface of the gland becoming more positive and then the hilus.

The two changes are believed to be due to the fact that secretory nerves are of two kinds: anabolic, which increase the building up of the glandular protoplasm; and katabolic, which increase the disintegrative side of metabolism, and so lead to secretion.

It is important to remember the existence of the skin currents, for they interfere with any attempt to determine the electrical change in muscles through the intact skin. This interference will naturally be greater, the richer the portion of skin is, in secreting glands.

The most satisfactory work on skin currents is that recently carried out by Waller. He speaks of them as glandular and epithelial, and regards them as important signs of life here as in other tissues (eye, muscle, nerve, plant tissues, etc.) which he has studied. He has worked with the skin of the frog, cat, and other animals, including fresh human skin obtained from surgical operations. The skin may be excited either directly or indirectly through the nerves that supply it. The main results obtained are very simple, and are also true for mucous membranes, and such epithelial structures as the crystalline lens. The normal current of unexcited living skin is ingoing. The normal response of excited skin is outgoing. This is explained in the following way:—In a passive mass of living animal material acted upon by its environment, there must be most change occurring on its surface, a point on the surface will therefore be electropositive to any point in the interior. If the same mass is excited, chemical changes will be greater in its interior than at the surface; hence internal points become less electronegative than they were before, or even electropositive in relation to the external surface, hence the current of action through the mass of skin is outgoing, and will therefore pass through the galvanometer from the external to the internal surface.

CHAPTER XXX

SALIVA

THE saliva is formed by three pairs of salivary glands, called the parotid, submaxillary, and sublingual glands.

The Salivary Glands.

These are typical secreting glands. They are made up of *lobules* united by connective tissue. Each lobule is made of a group of tubulo-saccular *alveoli* or *acini*, from which a duct passes; this unites with other ducts to form larger and larger tubes, the main duct opening into the mouth.

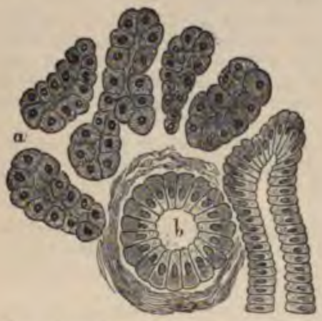

Fig. 393.—From a section through a salivary gland. *a*, serous or albuminous alveoli; *b*, intralobular duct cut transversely. (Klein and Noble Smith.)

Each alveolus is surrounded by a plexus of capillaries; the lymph which exudes from these is in direct contact with the basement membrane that encloses the alveolus. The basement membrane is lined by secreting cells which surround the central cavity or lumen. The basement membrane is thin in many places, to allow the lymph more ready access to the secreting cells; it is continued along the ducts.

The secreting epithelium is composed of a layer of polyhedral cells.

The epithelium of the ducts is columnar, except where it passes into an alveolus; at this point it is flattened. The columnar epithelium cells of the ducts exhibit striations in their outer part (see fig. 393); the inner zone of each cell is made of granular protoplasm. The largest ducts have a wall of connective tissue outside the basement-membrane, and a few unstriated muscular fibres.

The secreting cells differ according to the substance they secrete. In alveoli that secrete mucin (such as those in the dog's submaxillary, and some of the alveoli in the human submaxillary) the cells after treatment with water or alcohol are clear and swollen (fig. 395); this is the appearance they usually present in sections of the organ. But if examined in their natural state by teasing a portion of the fresh gland in serum, they are seen to be occupied by large granules composed of a substance known as *mucigen* or *mucinogen*. When the gland is active, mucigen is transformed into mucin and discharged as a clear droplet of that substance into the lumen of the alveolus. Outside these are smaller, highly granular cells containing no mucigen; these marginal cells stain darkly, and generally form crescentic groups (*crescents* or *demilunes* of Gianuzzi) next to the basement membrane. They do not secrete mucin, but are albuminous cells. After secretion their granules are lessened.

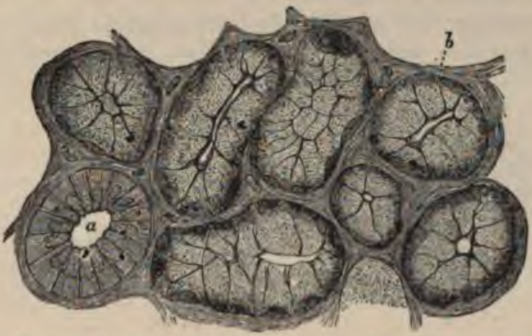

FIG. 394.—Section of submaxillary gland of dog. Showing gland-cells, *b*, and a duct, *a*, *b*, in section. (Kölliker.)

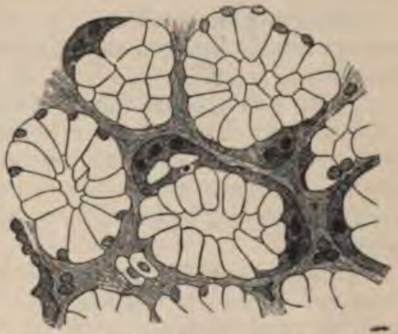

FIG. 395.—Section through a mucous gland hardened in alcohol. The alveoli are lined with transparent mucous cells, and outside these are the demilunes. (Heidenhain.)

In those alveoli which do not secrete mucin, but a watery non-viscid saliva (parotid, and some of the alveoli of the human submaxillary), the cells are filled with small granules of albuminous nature. Such alveoli are called *serous* or *albuminous*, to distinguish them from the *mucous* alveoli we have just described.

These yield to the secretion its ferment, *ptyalin*. The granular substance within the cell is the mother substance of the ferment (*zymogen*), not the ferment itself. It is converted into the ferment in the act of secretion. We shall study the question of zymogens more fully in connection with the gastric glands and the pancreas where they have been separated from the ferments by chemical methods. In the case of saliva we may term the zymogen, *ptyalinogen* provisionally, but it has never been satisfactorily separated chemically from ptyalin.

After secretion, due to the administration of food or of such a drug as pilocarpine, the cells shrink, they stain more readily, their nuclei become more conspicuous, and the outer part of each cell becomes clear and free from granules (fig. 396).

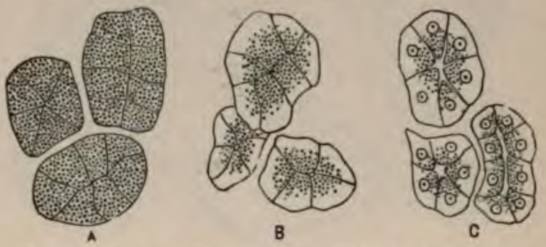

FIG. 396.—Alveoli of parotid gland. A, before secretion; B, in the first stage of secretion; C, after prolonged secretion. (Langley.)

The Secretory Nerves of Salivary Glands.

The nerve-fibres which are derived from cranial and sympathetic nerves ramify between the gland-cells, but have never actually been traced into them.

These nerves control and regulate the secretion of saliva.

The general truth concerning the existence of secretory nerves, we have already become acquainted with (p. 162). The subject has been worked out most thoroughly in connection with the salivary glands, particularly the submaxillary gland of the dog, which we will take first.

The Submaxillary and Sublingual Glands.—These glands receive two sets of nerve-fibres; namely, from the chordi tympani and the sympathetic.

The *chorda tympani* is given off from the seventh cranial nerve in the region of the tympanum.* After quitting the temporal bone it passes downwards and forwards, and joins the lingual nerve, with which it is bound up for a short distance. On leaving the lingual nerve it traverses the *submaxillary ganglion;* it then runs parallel to the duct of the gland, gives off a branch to the sublingual gland, and others to the tongue. The main nerve enters the hilus of the submaxillary gland, where it traverses a second ganglion concealed within the substance of the gland, and which may be called after its discoverer, *Langley's ganglion*.

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* Though the chorda tympani is usually spoken of as a branch of the seventh nerve, it is probable that some of its sensory fibres are derived from the glossopharyngeal; the origin of its secretory fibres is not known.

The *sympathetic* branches to these two glands are derived from the plexus around the facial artery, and accompany the arteries which supply the glands.

Section of the nerves produces no immediate result; but after a few days an abundant secretion of thin watery saliva takes place; this is called *paralytic secretion*, and is produced either by the activity of the local nervous mechanism, which is then uncontrolled by impulses from the central nervous system; or else, it is a degenerative effect analogous to the fibrillar contractions which occur in degenerating muscles after severance of their nerves. If the operation is performed on one side, the glands of the opposite side also show a similar condition, and the thin saliva secreted there is called the *antilytic* secretion.

Stimulation of the peripheral end of the divided chorda tympani produces an abundant secretion of saliva, which is accompanied by vaso-dilatation (see p. 306). Stimulation of the peripheral end of the divided sympathetic causes a scanty secretion of thick viscid saliva, accompanied by vaso-constriction.

The abundant secretion of saliva, which follows stimulation of the chorda tympani, is not merely the result of a filtration of fluid from the blood-vessels, in consequence of the largely increased circulation through them. This is proved by the fact that, when the main duct is obstructed, the pressure within it may considerably exceed the blood-pressure in the arteries,* and also that when into the veins of the animal experimented upon, some *atropine* has been previously injected, stimulation of the peripheral end of the divided chorda produces all the vascular effects as before, without any secretion of saliva accompanying them. Again, if an animal's head is cut off, and the chorda be rapidly exposed and stimulated with an interrupted current, a secretion of saliva ensues for a short time, although the blood-flow is necessarily absent. These experiments serve to prove that the chorda contains two sets of nerve-fibres, one set (*vaso-dilator*) which, when stimulated, cause the vessels to dilate; while another set, which are paralysed by atropine, directly stimulate the cells themselves to activity, whereby they secrete and discharge the constituents of the saliva which they produce. On the other hand, the sympathetic fibres are also of two kinds, vaso-constrictor and secretory, the latter being paralysed by atropine. The chorda tympani nerve is, however, the principal nerve through which efferent impulses proceed from the central nervous system to excite the secretion of these glands.

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* The student should not suppose that the saliva is normally secreted at such high pressure. If it were so the saliva would spurt from the salivary duct with greater force than the blood would spurt from the arteries when they are cut. The high pressure alluded to in the text only occurs when the duct is obstructed, and indicates what enormous force the secreting cells can exercise.

The function of the ganglia has been made out by Langley by the nicotine method (see p. 302). At one time the submaxillary ganglion was supposed to be the seat of reflex action for the secretion. This, however, is not the case. The ganglia are cell-stations on the course of the fibres to the submaxillary and sublingual glands. Nicotine applied locally has the power of paralysing nerve-cells, but not nerve-fibres. If the submaxillary ganglion is painted with nicotine, and the nerve stimulated on the central side of the ganglion, secretion from the submaxillary gland continues, but that from the sublingual gland ceases. The paralysed nerve-cells in the ganglion act as blocks to the propagation of the impulse, not to the submaxillary, but to the sublingual gland. The cell station for the submaxillary fibres is in Langley's ganglion.

Parotid Gland.—This gland also receives two sets of nerve-fibres analogous to those we have studied in connection with the submaxillary gland. The principal secretory nerve-fibres are glosso-pharyngeal in origin; the sympathetic is mainly vaso-constrictor, but in some animals does contain a few secretory fibres also.

When secretory nerves are stimulated, the main result is secretion leading to a diminution of the granules in the cells. The accompanying vascular condition determines the quantity of saliva secreted. Electrical changes also accompany secretory activity (see p. 473). A rise of temperature is stated to occur, but if this is the case it is very slight, and many observers have not been able to detect it.

Reflex Secretion.—Under ordinary circumstances the secretion of saliva is a reflex action. The principal afferent nerves are those of taste; but the smell or sight of food will also cause "the mouth to water"; and under certain circumstances, as before vomiting, irritation of the stomach has a similar effect. These sensory nerves stimulate a centre in the medulla from which efferent secretory impulses are reflected along the secretory nerves (chorda tympani, etc.) to the glands.

Pawlow has made some interesting observations on the salivary glands. He made an external fistula of the submaxillary duct in the dog, and found that the sight of food, the smell of food, or the administration of any kind of food, caused secretion; acid or even sand introduced into the mouth produced a similar effect. By means of similar experiments on the parotid secretion, very different results were obtained. If the dog was shown meat, or the meat was given to it to eat, there was practically no secretion. If, however, the meat was given as a dry powder, a copious secretion followed; dry bread produced a similar effect; in fact, the parotid secretion flows freely if dry food is simply shown to the animal; of course, in all such experiments, the dog must be hungry.

Such observations bring the salivary secretion into line with the other digestive juices; they show the psychical element involved, and point out also the wonderful adaptation of the secretory process to the needs of the animal; thus the submaxillary saliva, which is mainly a lubricant in virtue of its mucin, flows whatever the food may be, whereas moist food requiring no watery saliva from the parotid excites the flow of none.

Extirpation of the Salivary Glands.—These may be removed without any harmful effects in the lower animals.

The Saliva.

The **saliva** is the first digestive juice to come in contact with the food. The secretions from the different salivary glands differ somewhat in composition, but they are mixed in the mouth; the secretion of the minute mucous glands of the mouth and a certain number of epithelial cells and *débris* are added to it. The so-called "salivary corpuscles" are derived from the glands themselves or from the tonsils.

On microscopic examination of mixed saliva a few epithelial scales from the mouth and salivary corpuscles from the salivary glands are seen. The liquid is transparent, slightly opalescent, of slimy consistency, and may contain lumps of nearly pure mucin. On standing it becomes cloudy owing to the precipitation of calcium carbonate, the carbonic acid, which held it in solution as bicarbonate, escaping.

Of the three forms of saliva which contribute to the mixture found in the mouth the sublingual is richest in solids (2·75 per cent.). The submaxillary saliva comes next (2·1 to 2·5 per cent.). When artificially obtained by stimulation of nerves in the dog the saliva obtained by stimulation of the sympathetic is richer in solids than that obtained by stimulation of the chorda tympani. The parotid saliva is poorest in total solids (0·3 to 0·5 per cent.), and contains no mucin. Mixed saliva contains in man an average of about 0·5 per cent. of solids: it is alkaline in reaction, due to the salts in it; and has a specific gravity of 1002 to 1006.

The solid constituents dissolved in saliva may be classified thus:

Organic .	*a.* Mucin: this may be precipitated by acetic acid.
	b. Ptyalin: an amylolytic ferment.
	c. Proteid: of the nature of a globulin.
	d. Potassium sulphocyanide.
Inorganic .	*e.* Sodium chloride: the most abundant salt.
	f. Other salts: sodium carbonate, calcium phosphate and carbonate: magnesium phosphate; potassium chloride.

The action of saliva is twofold, physical and chemical.

The physical use of saliva consists in moistening the mucous membrane of the mouth, assisting the solution of soluble substances in the food, and in virtue of its mucin, lubricating the bolus of food to facilitate swallowing.

The chemical action of saliva is due to its active principle, ptyalin. This substance belongs to the class of unorganised ferments, and to that special class of unorganised ferments which are called amylolytic (starch splitting) or diastatic (resembling diastase, the similar ferment in germinating barley and other grains).

The starch is first split into dextrin and maltose; the dextrin is subsequently converted into maltose also: this occurs more quickly with erythro-dextrin, which gives a red colour with iodine, than with the other variety of dextrin called achroo-dextrin, which gives no colour with iodine. Brown and Morris give the following equation:—

$$\underset{\text{[Starch.]}}{10(C_6H_{10}O_5)n} + \underset{\text{[Water.]}}{4nH_2O}$$

$$= \underset{\text{[Maltose.]}}{4nC_{12}H_{22}O_{11}} + \underset{\text{[Achroo-dextrin.]}}{(C_6H_{10}O_5)_n} + \underset{\text{[Erythro-dextrin.]}}{(C_6H_{10}O_5)_n}.$$

Ptyalin acts in a similar way, but more slowly on glycogen: it has no action on cellulose; hence it is inoperative on uncooked starch grains, for in them the cellulose layers are intact.

Ptyalin acts best at about the temperature of the body (35-40° C.). It acts best in a neutral medium; a small amount of alkali makes but little difference; a very small amount of acid stops its activity. The conversion of starch into sugar by swallowed saliva in the stomach continues for a certain time. It then ceases owing to the hydrochloric acid secreted by the glands of the stomach. The acid which is first poured out neutralises the saliva, and combines with the proteids of the food, but when free acid appears ptyalin is destroyed, and so it cannot resume work when the acid is neutralised in the duodenum. Another amylolytic ferment contained in pancreatic juice (to be considered later) continues the digestion of starch in the intestine.

Cannon has recently shown that salivary digestion continues in the stomach for longer than one supposed. The food lying in the fundus of the stomach undergoes amylolysis for at least two hours, because the absence of peristalsis in this region until quite late stages in digestion prevents admixture with gastric juice, especially in the interior of the swallowed masses.

CHAPTER XXXI

THE GASTRIC JUICE

THE juice secreted by the glands in the mucous membrane of the stomach varies in composition in the different regions, but the mixed gastric juice, as it may be termed, is a solution of a proteolytic ferment called *pepsin* in a saline solution, which also contains a little free hydrochloric acid.

The gastric juice can be obtained during the life of an animal by means of a gastric fistula.* Gastric fistulæ have also been made in human beings, either by accidental injury or by surgical operations. The most celebrated case is that of Alexis St Martin, a young Canadian, who received a musket wound in the abdomen in 1822. Observations made on him by Dr Beaumont formed the starting-point for our correct knowledge of the physiology of the stomach and its secretion.

We now make artificial gastric juice by mixing weak hydrochloric acid (0·2 per cent.) with the glycerin extract of the stomach of a recently-killed animal. This artificial juice acts like the normal juice.

Two kinds of glands are distinguished in the stomach, which differ from each other in their position, in the character of their epithelium, and in their secretion. Their structure will be found described on pp. 449, 451. We may, however, repeat that the *cardiac glands* are those situated in the cardiac part of the stomach: their ducts are short, their tubules long in proportion. The latter are filled with polyhedral cells, only a small lumen being left; they are more coarsely granular than the corresponding cells in the pyloric glands. They are called *principal* or *central* cells. Between them and the basement membrane of the tubule are other cells which stain readily with aniline dyes. They are called *parietal* or *oxyntic* cells. The

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* A gastric fistula is made by cutting through the abdominal wall so as to expose the stomach. The stomach is then attached to the edges of the abdominal wound, and a small orifice is finally made through the wall of the stomach. When the wound heals there is then a free communication between the stomach and the exterior.

pyloric glands, in the pyloric part of the stomach, have long ducts and short tubules lined with cubical granular cells. There are no parietal cells.

The **central** cells of the cardiac glands and the cells of the pyloric glands are loaded with granules. During secretion they discharge their granules, those that remain being chiefly situated near the lumen, leaving in each cell a clear outer zone. These are the cells that secrete the pepsin. Like secreting cells generally, they select certain materials from the lymph that bathes them; these materials are worked up by the protoplasmic activity of the cells into the secretion, which is then discharged into the lumen of the gland. The most important substance in a digestive secretion is the ferment. In the case of the gastric juice this is pepsin. We can trace an intermediate step in this process by the presence of the granules. The granules are not, however, composed of pepsin, but of a mother-substance which is readily converted into pepsin. We shall find a similar ferment precursor in the cells of the pancreas, and the term *zymogen* is applied to these ferment precursors. The zymogen in the gastric cells is called *pepsinogen.* The rennet-ferment or rennin that causes the curdling of milk is distinct from pepsin, but is formed by the same cells.

The **parietal cells** undergo merely a change of size during secretion, being at first somewhat enlarged, and after secretion they are somewhat shrunken. They are also called *oxyntic* (acid-forming) cells, because they secrete the hydrochloric acid of the juice. Heidenhain succeeded in making in one dog a *cul-de-sac* of the fundus, in another of the pyloric region of the stomach; the former secreted a juice containing both acid and pepsin; the latter, parietal cells being absent, secreted a viscid alkaline juice containing pepsin. The formation of a free acid from the alkaline blood and lymph is an important problem. There is no doubt that it is formed from the chlorides of the blood and lymph, and of the many theories advanced as to how this is done, Maly's is, on the whole, the most satisfactory. He considers that it originates by the interaction of the calcium chloride with the di-sodium hydrogen phosphate of the blood, thus:—

$$\underset{\substack{\text{[Di-sodium hydrogen}\\ \text{phosphate.]}}}{2Na_2HPO_4} + \underset{\substack{\text{[Calcium}\\ \text{chloride.]}}}{3CaCl_2} = \underset{\substack{\text{[Calcium}\\ \text{phosphate.]}}}{Ca_3(PO_4)_2} + \underset{\substack{\text{[Sodium}\\ \text{chloride.]}}}{4NaCl} + \underset{\substack{\text{[Hydrochloric}\\ \text{acid.]}}}{2HCl},$$

or more simply by the interaction of sodium chloride and sodium di-hydrogen phosphate, as is shown in the following equation:—

$$\underset{\substack{\text{[Sodium di-hydrogen}\\ \text{phosphate.]}}}{NaH_2PO_4} + \underset{\substack{\text{[Sodium}\\ \text{chloride.]}}}{NaCl} = \underset{\substack{\text{[Di-sodium hydrogen}\\ \text{phosphate.]}}}{Na_2HPO_4} + \underset{\substack{\text{[Hydro-}\\ \text{chloric acid.]}}}{HCl}.$$

The sodium di-hydrogen phosphate in the above equation is derived from the interaction of the di-sodium hydrogen phosphate and the carbonic acid of the blood, thus:—

$$Na_2HPO_4 + CO_2 + H_2O = NaHCO_3 + NaH_2PO_4.$$

But, as Gamgee has pointed out, these reactions can hardly be considered to occur in the blood generally, but rather in the oxyntic cells, which possess the necessary selective powers in reference to the saline constituents of the blood, and the hydrochloric acid, as soon as it is formed, passes into the secretion of the gland in consequence of its high power of diffusion.

Composition of Gastric Juice.

The following table gives the percentage composition of the gastric juice of man and the dog:—

Constituents.	Human.	Dog.
Water	99·44	97·30
Organic substances (chiefly pepsin)	0·32	1·71
HCl	0·20	0·40 to 0·60
$CaCl_2$	0·006	0·06
$NaCl$	0·14	0·25
KCl	0·05	0·11
NH_4Cl	...	0·05
$Ca_3(PO_4)_2$	0·01	0·17
$Mg_3(PO_4)_2$		0·02
$FePO_4$		0·008

One sees from this how much richer in all constituents the gastric juice of the dog is than that of man. Carnivorous animals have always a more powerful gastric juice than other animals; they have more work for it to do; but the great contrast seen in the table is, no doubt, partly due to the fact that the persons from whom it has been possible to collect gastric juice have been invalids. In the foregoing table one also sees the great preponderance of chlorides over other salts; apportioning the total chlorine to the various metals present, that which remains over must be combined with hydrogen to form the free hydrochloric acid of the juice.

In recent years, the composition and action of the gastric juice has been studied by Pawlow. By an ingenious surgical operation, he succeeded in separating from the stomach of dogs a diverticulum which pours its secretion through an opening in the abdominal wall; the nerves of this small stomach are intact, and the amount of juice that can be collected from it when it is active amounts to several hundred cubic centimetres in a few hours. Pawlow thus obtained a pure gastric juice, which enabled him to study its action and composition. It is clear, colourless, has a specific gravity of 1003—1006, and is feebly dextro-rotatory. It contains 0·4 to 0·6 per cent. of hydrochloric acid. It is strongly proteolytic, and inverts cane sugar. When cooled to 0° C. it deposits a precipitate of pepsin, and this carries down with it the acid in loose combination, especially in the layers first deposited. Its percentage composition is very similar to that of a proteid, only it contains chlorine in addition to the usual elements. The numbers agree closely with those obtained by Kühne, who used ammonium sulphate as the precipitant. The following are the analytical figures:—

	Pepsin precipitated by cold.	Precipitated by Am_2SO_4.
	Per cent.	Per cent.
Carbon	50·73	50·37
Hydrogen	7·23	6·88
Chlorine	1·01 to 1·17	0·89
Sulphur	0·98	1·34
Nitrogen	Not estimated	14·55 to 15·0
Oxygen	The remainder	The remainder.

Pepsin stands apart from nearly all other ferments by requiring an acid medium in order that it may act. Probably a compound of the two substances, called *pepsin-hydrochloric acid*, is the really active agent. Other acids may take the place of hydrochloric acid, but none act so well. Lactic acid is often found in gastric juice: this is derived by fermentative processes from the food.

The digestive powers of the acids are proportional to their dissociation and the number of H ions liberated. The anions, however, modify this by having different powers of retarding the action. The greater suitability of hydrochloric over lactic acid, for instance, in gastric digestion is due to the fact that the former acid more readily undergoes dissociation.

Hydrochloric acid is absent in some diseases of the stomach; the best colour tests for it are the following:—

(*a*) Gunsberg's reagent consists of 2 parts of phloroglucinol, 1 part of vanillin, and 30 parts of rectified spirit. A drop of filtered gastric juice is evaporated with an equal quantity of the reagent. Red crystals form, or if much peptone is present, there will be a red paste. The reaction takes place with one part of hydrochloric acid in 10,000. The organic acids do not give the reaction.

(*b*) Tropæolin test. Drops of a saturated solution of tropæolin -00 in 94 per cent. methylated spirit are allowed to dry on a porcelain slab at 40° C. A drop of the fluid to be tested is placed on the tropæolin drop, still at 40° C.; and if hydrochloric acid is present, a violet spot is left when the fluid has evaporated. A drop of 0·006 per cent. hydrochloric acid leaves a distinct mark.

(*c*) Töpfer's test. A drop of dimethyl-amido-azo-benzol is spread in a thin film on a white plate. A drop of dilute hydrochloric acid (up to 1 in 10,000) strikes with this in the cold a bright red colour.

Lactic acid is soluble in ether, and is generally detected by making an ethereal extract of the stomach contents, and evaporating the ether. If lactic acid is present in the residue it may be identified by the following way:—

A solution of dilute ferric chloride and carbolic acid is made as follows:—

10 c.c. of a 4-per-cent. solution of carbolic acid.

20 c.c. of distilled water.

1 drop of the liquor ferri perchloridi of the British Pharmacopœia.

On mixing a solution containing a mere trace (up to 1 part in 10,000) of lactic acid with this violet solution, it is instantly turned yellow. Larger percentages of other acids (for instance, more than 0·2 per cent. of hydrochloric acid) are necessary to decolorise the test solution.

The Innervation of the Gastric Glands.

As long ago as 1852 Bidder and Schmidt showed in a dog with a gastric fistula that the sight of food caused a secretion of gastric juice; and in 1878 Richet observed that in a man with complete occlusion of the gullet the act of mastication caused a copious flow of gastric juice. There could therefore have been no doubt that the glands are under the control of the nervous system, but the early attempts to discover the secretory nerves of the stomach were unsuccessful. The Russian physiologist Pawlow has solved the problem by the employment of new methods. He experimented on dogs. In the first place he separated off the diverticulum, which we have described on p. 483, and by careful experiments he showed that the secretion of this small stomach is an exact sample, both as regards composition and rate of formation, of that which occurs in the main stomach, which is still left in continuity with the œsophagus above and the duodenum below.

Another procedure adopted was to divide the œsophagus, and to attach the two cut ends to the opening in the neck. The animal was fed by the lower segment, but any food taken into the mouth, or any saliva secreted there, never reached the stomach, but fell out through the opening of the upper segment. These animals were kept alive for months, and soon accommodated themselves to their new conditions of life. The animals could thus be subjected to, (1) real feeding, (2) sham feeding, by allowing them to eat food which subsequently tumbled out through the neck opening, and (3) psychical feeding, in which the animal was shown the food but was not allowed to eat it. The psychical element is important.

Mechanical excitation of the stomach wall produces no secretion. If water is introduced there is a slight flow, and even if meat is introduced into the main stomach without the knowledge of the dog, the juice formed is scanty and of feeble digestive power.

There is, moreover, no connection between the acts of mastication and swallowing with that of gastric secretion. Sham feeding with stones, butter, salt, pepper, mustard, extract of meat, and acid, though it excited a flow of saliva, produced no effect on the stomach. If, however, meat was used for the sham feeding, an abundant and active secretion occurred in the stomach (that of the small stomach was actually examined) after a latency of about five minutes. The secretion is thus adapted to the kind of food the dog has to digest; the larger the proportion of proteid in the diet, the more abundant is the juice, and the richer both in pepsin and acid.

Indeed, if the animal is hungry and shown the meat and not allowed to swallow it, the effect is as great. The following striking experiment also shows the importance of the psychical element. Two dogs were taken, and a weighed amount of proteid introduced into the main stomach in each without their knowledge; one was then sham fed on meat, and one and a half hours later the amount of proteid digested by this dog was five times greater than that which was digested by the other.

In the meat, however, it is not the proteid which acts most strongly as the stimulus; egg-white, for instance, is not a stronger stimulus than water, but extract of meat is a powerful stimulus; what the exact extractives are that act in this way is not yet known, and Herzen has since shown that dextrin acts even more powerfully. Herzen distinguishes between *succagogues* (juice-drivers) like Liebig's extract, and *peptogens* like dextrin, which produce not only an increased flow, but a juice rich in pepsin-hydrochloric acid. The products of proteolysis are also peptogenic, so that when once digestion has started, a stimulus for more secretion is provided.

If the vagi are cut (below the origin of the recurrent laryngeal to avoid paralysis of the larynx), and then sham feeding is performed with meat, no secretion is obtained; the vagi therefore contain the secretory fibres. The experiment of stimulating the peripheral end of the cut nerve confirmed this hypothesis. The nerve was cut in the neck four or five days before it was stimulated; in this time degeneration of the cardio-inhibitory fibres took place, so that stoppage of the heart did not occur when the nerve was stimulated; under these circumstances a secretion was obtained with a long latency; the latency is explained by the presence of secreto-inhibitory fibres. Atropine abolishes the action of the vagus. In other animals the spinal cord was cut at the level of the first cervical nerve, and the animal kept alive by artificial respiration; the vagus nerve was then cut, and its peripheral end stimulated; an abundant secretion usually followed. Division of the cord renders an anæsthetic unnecessary, and also prevents the afferent impulses set up by the operation passing to the vagal centres, and thus exciting the inhibitory impulses which pass down the vagus, and tend to prevent secretion under ordinary circumstances.

Pawlow thinks that the sympathetic also contains some secretory fibres, but this has not yet been proved.

Action of Gastric Juice.

The principal action of the gastric juice consists in converting the proteids of the food into the diffusible peptones. In the case of milk this is preceded by the curdling due to rennet (see p. 462).

There is a still further action—that is, the gastric juice is antiseptic; putrefactive processes do not normally occur in the stomach, and the organisms that produce such processes, many of which are swallowed with the food, are in great measure destroyed, and thus the body is protected from them.

The formation of peptones is a process of hydrolysis; peptones may be formed by other hydrating agencies like superheated steam and heating with dilute mineral acids. There are certain intermediate steps in this process: the intermediate substances are called propeptones or proteoses. The word "proteose" includes the albumoses (from albumin), globuloses (from globulin), vitelloses (from vitellin), etc. Similar substances are also formed from gelatin (gelatinoses) and elastin (elastoses).

Another intermediate step in gastric digestion is called parapeptone: this is acid albumin or syntonin. The products of digestion of albumin may be classified, according to the order in which they are formed, as follows:—

1. **Parapeptone, or acid albumin.**
2. Propeptone
    - (*a*) **Proto-albumose** } **The primary albumoses, *i.e.*, those which are formed first.**
    - (*b*) **Hetero-albumose** }
    - (*c*) **Deutero-albumose**
3. Peptone.

It is doubtful whether all the proteid present passes through the acid-albumin stage.

The primary albumoses are precipitated by saturation with magnesium sulphate or sodium chloride. Deutero-albumose is not; it is, however, precipitated by saturation with ammonium sulphate. Proto- and deutero-albumose are soluble in water; hetero-albumose is not; it requires salt to hold it in solution.

Peptones.—They are soluble in water, are not coagulated by heat, and are not precipitated by nitric acid, copper sulphate, ammonium sulphate, and a number of other precipitants of proteids. They are precipitated but not coagulated by alcohol. They are also precipitated by tannin, picric acid, potassio-mercuric iodide, phospho-molybdic acid, and phospho-tungstic acid.

They give the biuret reaction (rose-red solution with a trace of copper sulphate and caustic potash or soda).

Peptone is readily diffusible through animal membranes. The utility of the formation of diffusible substances during digestion is obvious.

Proteoses.—They are not coagulated by heat; they are precipitated but not coagulated by alcohol: like peptone they give the biuret reaction. They are precipitated by nitric acid, *the precipitate being soluble on heating, and reappearing when the liquid cools.*

This last is a distinctive property of proteoses. They are slightly diffusible.

Variety of proteid.	Action of heat.	Action of alcohol.	Action of nitric acid.	Action of ammonium sulphate.	Action of copper sulphate and caustic potash.	Diffusibility.
Albumin	Coagulated	Precipitated, then coagulated	Precipitated in the cold; not readily soluble on heating	Precipitated by complete saturation	Violet colour	Nil
Globulin	Ditto.	Ditto.	Ditto.	Precipitated by half saturation; also precipitated by $MgSO_4$.	Ditto.	Ditto.
Proteoses (albumoses)	Not coagulated	Precipitated, but not coagulated	Precipitated in the cold; readily soluble on heating; the precipitate reappears on cooling*	Precipitated by saturation	Rose-red colour (biuret reaction)	Slight
Peptones	Not coagulated	Precipitated, but not coagulated	Not precipitated	Not precipitated	Rose-red colour (biuret reaction)	Great

The above table will give us at a glance the chief characters of peptones and proteoses in contrast with those of the native proteids, albumins, and globulins.

We see that the main action of the gastric juice is upon the proteids of the food, converting them into more soluble and diffusible products. The fats are not chemically altered in the stomach,† their proteid envelopes are, however, dissolved, and the solid fats are melted. Starch is unaffected; but cane sugar is inverted. The inversion of cane sugar is largely due to the hydrochloric acid of the juice, and is frequently assisted by inverting ferments contained in the vegetable food swallowed.

The question has been often raised why the stomach does not digest itself during life. The mere fact that the tissues are alkaline and pepsin requires an acid medium in which to act is not an explanation, but only opens up a fresh difficulty as to why the pancreatic juice which is alkaline does not digest the intestinal wall. To say that it is the vital properties of the tissues that enable them to resist digestion only shelves the difficulty and gives no real explanation of the mechanism of defence. Recent studies on the important question of immunity (see p. 439)

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[*] In the case of deutero-albumose this reaction only occurs in the presence of excess of salt.

[†] According to some recent observations, a small amount of fat-splitting does occur in the stomach.

have furnished us with the key to the problem; just as poisons introduced from without stimulate the cells to produce antitoxins, so harmful substances produced within the body are provided with anti-substances capable of neutralising their effects; for this reason the blood does not normally clot within the blood-vessels, and Weinland has shown that the gastric epithelium forms an antipepsin, the intestinal epithelium an antitrypsin, and so on.

Mett's Tubes.

A method which is now generally employed for estimating the proteolytic activity of a digestive juice is one originally introduced by Mett. Pieces of capillary glass tubing of known length are filled with white of egg. This is set into a solid by heating to 95° C. They are then placed in the digestive fluid at 36° C., and the coagulated egg-white is digested. After a given time the tubes are removed; and if the digestive process has not gone too far, only a part of the little column of coagulated proteid will have disappeared; the length of the remaining column is easily measured, and the length that has been digested is a measure of the digestive strength of the fluid.

Hamburger has used the same method in investigating the digestive action of juices on gelatin. The tubes are filled with warm gelatin solution, and this jellies on cooling. They are placed as before in the digestive mixture, and the length of the column that disappears can be easily measured. These experiments must, however, be performed at room temperature, for the usual temperature (36°—40° C.) at which artificial digestion is usually carried out would melt the gelatin. He has also used the same method for estimating amylolytic activity, by filling the tubes with thick starch paste.

Schütz' Law.

E. Schütz stated in 1885 that the amount of peptic activity is proportional to the square root of the amount of pepsin. This was confirmed by Borissow, who used Mett's capillary tube method. An example (taken from the work of E. Schütz, who estimated the amount of the digestive products in solution by means of nitrogen determinations) will suffice.

Amount of Solution of Pepsin in Cubic Centimetres.	Digested Nitrogen in Grammes.	
	Found.	Calculated.
1	0·0230	0·0223
4	0·0427	0·0446
9	0·0686	0·0669
16	0·0889	0·0892

This work was an early attempt to deal with enzyme action on exact mathematical lines, a branch of the subject now being extensively studied. Some have stated that the law holds more or less exactly for other enzymes; in other cases the relationship is different. The usual method now adopted is to estimate the velocity of reaction, that is, the time occupied by the ferment in accomplishing a given end on a fixed amount of material. If, for instance, one takes a series of tubes, each containing the same amount of milk, and adds to each different known amounts of rennet, the time occupied in producing curdling is accurately noted. In this case, and in similar experiments with blood or blood-plasma and fibrin ferment, the amount of ferment multiplied by the coagulation time is constant; thus, if two drops of rennet produce coagulation in 30 seconds, four drops will curdle the same amount of milk in 15 seconds. The same simple relationship also probably holds for the action of invertin, erepsin, and trypsin.

CHAPTER XXXII

DIGESTION IN THE INTESTINES

HERE we have to consider the action of pancreatic juice, of bile, and of the succus entericus.

The Pancreas.

This is a tubulo-racemose gland closely resembling the salivary glands in structure. The principal differences are that the alveoli or acini are more tubular in character; the connective tissue between them is looser, and in it are small groups of epithelium-like cells, which are supplied by a close network of capillaries (fig. 398).

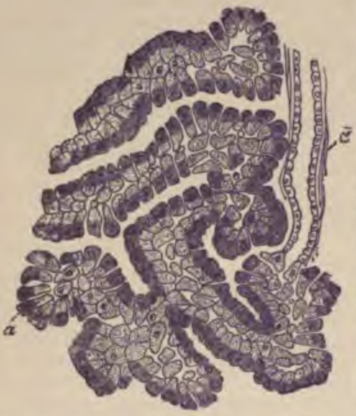

FIG. 397.—Section of the pancreas of a dog during digestion. *a*, alveoli lined with cells, the clear outer zone of which is well stained with hæmatoxylin; *d*, duct lined with short cubical cells. × 350. (Klein and Noble Smith.)

The secreting cells of the pancreas are polyhedral. When examined in the fresh condition, or in preparations preserved by osmic acid, their protoplasm is seen to be filled in the inner two-thirds with small granules; but the outer third is left clear, and stains readily with protoplasmic dyes (fig. 397).

During secretion the granules are discharged; the clear zone consequently becomes wider, and the granular zone narrower.

These granules indicate the presence of a zymogen which is called *trypsinogen;* that is, the precursor of trypsin, the most important ferment of the pancreatic juice.

In the centre of the acini, spindle-shaped cells (*centro-acinar* cells) are often seen; their function and origin are unknown.

Composition and Action of Pancreatic Juice.

The pancreatic juice may be obtained by a fistula in animals, a cannula being inserted into the main pancreatic duct; but as in the case of gastric juice, experiments on the pancreatic secretion are usually performed with an artificial juice made by mixing a weak alkaline solution (1 per cent. sodium carbonate) with a glycerin extract of pancreas. The pancreas should be treated with dilute acid for a few hours before the glycerin is added. This ensures a conversion of the trypsinogen into trypsin.

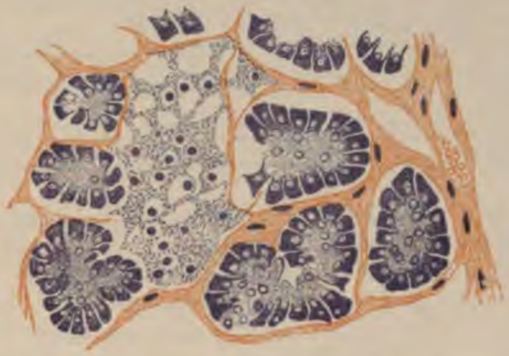

FIG. 398.—Section of the pancreas of armadillo, showing alveoli and an islet of Langerhans in the connective tissue. (V. D. Harris.)

Quantitative analysis of human pancreatic juice gives the following results:—

Water	97·6 per cent.
Organic solids	1·8 ,,
Inorganic salts	0·6 ,,

In the dog the amount of solids is much greater.

The organic substances in pancreatic juice are—

(*a*) Ferments. These are the most important both quantitatively and functionally. They are four in number:—

i. Trypsin, a proteolytic ferment.
ii. Amylopsin or pancreatic diastase, an amylolytic ferment.
iii. Steapsin, a fat-splitting or lipolytic ferment.
iv. A milk-curdling ferment.

(*b*) A small amount of proteid matter, coagulable by heat.

(*c*) Traces of leucine, tyrosine, xanthine, and soaps.

The inorganic substances in pancreatic juice are—

Sodium chloride, which is the most abundant, and smaller quantities of potassium chloride, and phosphates of sodium, calcium, and magnesium. The alkalinity of the juice is due to phosphates and carbonates, especially of sodium.

1. **Action of Trypsin.**—Trypsin acts like pepsin, but with certain differences, which are as follows:—

(*a*) It acts in an alkaline, pepsin in an acid medium.

(*b*) It acts more rapidly than pepsin; deutero-proteoses can be detected as intermediate products in the formation of peptone; the primary proteoses have not been detected.

(*c*) An albuminate of the nature of alkali-albumin is formed in place of the acid-albumin of gastric digestion.

(*d*) It acts more powerfully on certain albuminoids (such as elastin) which are difficult of digestion in gastric juice. It does not, however, digest collagen.

(*e*) Acting on solid proteids like fibrin, it eats them away from the surface to the interior; there is no preliminary swelling as in gastric digestion.

(*f*) Trypsin acts further than pepsin, on prolonged action decomposing the peptone which has left the stomach into simpler products, of which the most important are leucine, tyrosine (see p. 499), polypeptides (see p. 500), arginine (see p. 404), aspartic acid [amino-succinic acid $C_2H_3(NH_2)(COOH)_2$], glutamic acid [amino-pyrotartaric acid, $C_3H_5(NH_2)(COOH)_2$], ammonia, and a substance called tryptophan [indole-amino-propionic acid], which gives a red colour with chlorine or bromine water, and also the Adamkiewicz reaction (p. 398).

The action of proteolytic enzymes is, by a process of hydrolysis, to split the heavy proteid molecule into smaller and smaller molecules; first, we get proteoses, then peptones and polypeptides, and, finally, simple products like leucine and tyrosine. A variable fraction of the proteid molecule is broken off with comparative ease, but the whole breakdown is more easily performed by the powerful tryptic enzyme than by the comparatively feeble agent pepsin. Pepsin, however, is not entirely inactive in this direction, for although leucine and tyrosine are not usually found in a peptic digest, unless the action has been very prolonged, yet there are analogous substances of low molecular weight (aspartic acid, hexone bases, etc.), which were incorrectly grouped together by the earlier workers as a peptone (antipeptone). The essential difference between pepsin and trypsin is one of velocity of action.

2. **Action of Amylopsin.**—The conversion of starch into maltose is the most powerful and rapid of all the actions of the pancreatic juice. It is much more powerful than saliva, and will act even on unboiled starch. The absence of this ferment in the pancreatic juice of infants is an indication that milk, and not starch, is their natural diet.

3. **Action on Fats.**—The action of pancreatic juice on fats is a double one: it forms an *emulsion,* and it decomposes the fats into fatty acids and glycerin by means of its fat-splitting ferment steapsin. The fatty acids unite with the alkaline bases to form soaps (*saponification*). The chemistry of this is described on p. 395. The fat-splitting power of pancreatic juice cannot be studied with a glycerin

extract, as steapsin is not soluble in glycerin: either the fresh juice or a watery extract of pancreas must be used.

The formation of an emulsion may be studied in the following way: if olive oil and water are shaken up together, and the mixture is allowed to stand, the finely divided oil globules soon separate, run together, and form a layer which floats on the surface of the water. But if olive oil is shaken up with a solution of soap, the conditions of surface tension are such that the oil globules remain as such in the mixture, and a white milky fluid called an emulsion is the result. The emulsion is still more permanent if a colloid material like gum or albumin is also present. Pancreatic juice possesses all the necessary qualifications for the formation of an emulsion; it is alkaline, and so liberates fatty acids from the fat; these acids form soap with the alkali present; moreover, it is viscous from the presence of proteid.

4. **Milk-curdling Ferment.**—The addition of pancreatic extracts or pancreatic juice to milk causes clotting; but this action (which differs in some particulars from the clotting caused by rennet) can hardly ever be called into play, as the milk upon which the juice has to act has been already curdled by the rennin of the stomach.

Secretory Nerves of the Pancreas.

It has been known since the work of Claude Bernard in 1856 that the introduction of ether into the stomach produces a reflex flow of pancreatic juice, but all attempts to discover the path of the nerve impulses failed until the recent work of Pawlow. The reason of the failure of previous workers is that the pancreas is remarkably sensitive to external conditions. If the pancreas is cooled or wounded during the process of making the fistula, or if sensory nerves are excited, or if anæsthesia is deep, the gland refuses to secrete.

Pawlow discovered that the vagus contains the secretory nerves of the pancreas; he took care to avoid the sources of error just referred to. In the first place, he stimulated the vagi below the origin of their cardiac branches; in the second, the spinal cord was divided high up to prevent reflexes occurring from sensory nerves; and lastly, the operation of stimulating the nerve was done without an anæsthetic.

In another series of experiments, he cut through one vagus in the neck, and stimulated the peripheral end two or three days later, when the cardio-inhibitory fibres had degenerated: in this way he got rid of the heart stoppage, which would have interfered with the normal condition of the animal.

The stimulation of the vagus usually produced an abundant flow of pancreatic juice, after a latent period of from fifteen seconds to two minutes. The stimulation applied to the nerve consisted of a slow series of shocks (either induction currents or mechanical blows) about once a second. By this means stimulation of vaso-constrictor nerves to the pancreas contained in the vagus is avoided. If the blood supply is diminished by stimulation of vaso-constrictor nerves, the secretion is stopped.

In connection with Pawlow's interesting results, it is desirable to add some more details. The juice was obtained from dogs by stitching the portion of the intestinal wall that contained the orifice of the main pancreatic duct to the abdominal wall, in such a way that the juice was poured to the exterior and could be readily collected. If both vagi are prepared, stimulation of one causes secretion after a latent period which may amount to as much as fifteen minutes. If, then, while the juice is flowing, the opposite vagus is stimulated, the secretion is at once arrested; this shows the existence of secreto-inhibitory fibres, which it will be remembered is also the case with the stomach. One of the most effective ways of producing a flow of pancreatic juice is to introduce acid into the duodenum, and no doubt the acid gastric juice under normal circumstances is the stimulus for the pancreatic flow. If while the juice so produced is flowing, the vagus is stimulated, partial inhibition occurs in all cases.

The existence of secretory fibres in the sympathetic for the gastric glands is uncertain, but they certainly are present for the pancreas.

If the branches of nerves that actually enter the pancreas are stimulated, it is possible to differentiate between the secretory and the inhibitory fibres, for the excitation of some branches give mainly secretion, and of others mainly inhibition.

We may next compare the pancreatic to the gastric secretion, and we shall see how beautifully adjusted is the mechanism to the work it has to do.

The amount of gastric juice rises to a maximum at the end of the first hour, and then slowly falls to zero, which it reaches at the fifth hour after the meal. The pancreatic secretion rises to its maximum when it is most wanted—namely, later, *i.e.*, at the end of the third hour, and falls to zero at the end of the fifth hour.

The digestive power of the juices varies with the kind of food given. Thus with gastric juice, if the proteolytic activity when milk (a readily digestible food) is given be taken as 1, that when meat is given is 1½, and when bread is given it rises to 4, the proteid of bread being relatively very insoluble. The total acid secreted is, however, greatest with meat and lowest with bread.

Using the same three typical foods, the results with pancreatic secretion are as follows:—

When meat is given, a large amount of pancreatic juice is secreted, with medium proteolytic power, and low diastatic and fat-splitting activity.

When bread is given, more juice is secreted; its fat-splitting action is very feeble; its proteolytic power, at first of medium strength, rapidly rises; and its diastatic action similarly increases quickly.

When milk is given, the juice first secreted has high proteolytic and diastatic properties; but these fall gradually, whereas the fat-splitting action is very great.

The so-called Peripheral Reflex Secretion of the Pancreas.

We have already seen that the introduction of acid into the duodenum causes a flow of pancreatic juice. Popielski and Wertheimer and Le Page showed that this flow still occurs when the nerves supplying the duodenum and pancreas have been cut through. Wertheimer also mentions that the flow can be excited by injection of acid into the jejunum, but not when it is injected into the lower part of the ileum. These authors conclude that the secretion is a local reflex, the centres being situated in the scattered ganglia of the pancreas, or, in the case of the jejunum, in the ganglia of the solar plexus.

This subject has been re-investigated by Starling and Bayliss, and the results they have obtained are most noteworthy. They consider that the secretion cannot be reflex, since it occurs after extirpation of the solar plexus, and destruction of all nerves passing to an isolated loop of jejunum. Moreover, atropine does not paralyse the secretory action. It must therefore be due to direct excitation of the pancreatic cells, by a substance or substances conveyed to the gland from the bowel by the blood-stream. So many of the connections between organs are made by nerves (the telegraphic service of the body), that we are apt to forget the other messenger, the blood, whom we may compare to the postman.

The exciting substance is not acid; injection of 0·4 per cent. of hydrochloric acid into the blood-stream has no influence on the pancreas. The substance in question must be produced in the intestinal mucous membrane under the influence of the acid. This conclusion was confirmed by experiment If the mucous membrane of the jejunum or duodenum is exposed to the action of 0·4 per cent. hydrochloric acid, a body is produced which, when injected into the blood-stream in minimal doses, produces a copious secretion of pancreatic juice. This substance is termed *secretin*. It is associated with another substance which lowers arterial blood-pressure. The two substances are not identical, since acid extracts of the lower end of the ileum produce a lowering of blood-pressure, but have no excitatory influence on the pancreas.

Secretin is split off from a precursor, *pro-secretin*, which is present in relatively large amounts in the duodenal mucous membrane, and gradually diminishes as we descend the intestine. Pro-secretin can be dissolved out of the mucous membrane by normal saline solution. It has no influence on the pancreatic secretion. Secretin can be split off from it by boiling or by treatment with acid.

What secretin is chemically we do not yet know. It is soluble in alcohol and ether. It is not a proteid, but probably is an organic substance of low molecular weight. It is, moreover, the same substance in all animals, and not specific to different kinds of animals.

Whether this discovery is an isolated instance of chemical sympathy between different organs, or whether it is only one of a class of similar mechanisms, must be left to the future. It certainly shows that some revision of, or addition to, Pawlow's work is necessary. In none of Pawlow's experiments on the pancreas was a possible expulsion of acid from the stomach into the duodenum excluded.

The Succus Entericus.

Succus entericus has been obtained free from other secretions by means of a fistula. Thiry's method is to cut the intestine across in two places; the loop so cut out is still supplied with blood and nerves, as its mesentery is intact; this loop is emptied, one end is sewn up, and the other stitched to the abdominal wound, and so a *cul-de-sac* from which the secretion can be collected is made. The continuity of the remainder of the intestine is restored by fastening together the upper and lower portions of the bowel from which the loop has been removed. Vella's method resembles Thiry's, except that both ends of the loop are sutured to the wound in the abdomen. Fig. 399 illustrates the two methods.

The succus entericus possesses to a slight extent the power of converting starch into sugar. Its best known action is due to a ferment called *invertin*, which inverts saccharoses—that is, it converts cane sugar and maltose into glucose. The original use of the term "inversion" has been explained on p. 390. It may be extended to include the similar hydrolysis of other saccharoses, although there may be no formation of levo-rotatory substances. There are probably numerous inverting ferments, each of which acts on a different saccharose.

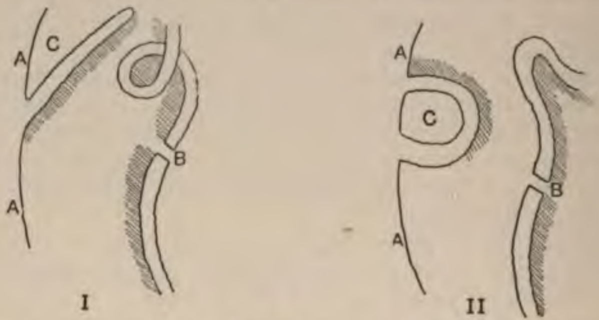

FIG. 399. Diagram of intestinal fistula. I., Thiry's method; II., Vella's method. A, abdominal wall; B, intestine with mesentery; C, separated loop of intestine, with attached mesentery.

Up till a year or two ago little or nothing was known regarding the action of the intestinal juice beyond this, but investigations published quite recently have, however, altered this state of things, and in the light of these the succus entericus appears to be a juice of the highest importance.

Pawlow was the first to show that one of its main actions is to reinforce and intensify the action of the pancreatic juice, especially in reference to its proteolytic power. Fresh pancreatic juice has practically no digestive power on proteids. Claude Bernard, the earliest to study the pancreatic secretion, entirely missed its tryptic action. On standing, the juice very slowly acquires proteolytic activity. Vernon has shown that much the same is true for extracts of the pancreas. There is no doubt that what the fresh juice contains is trypsinogen, and this is slowly transformed into the active enzyme trypsin.

If fresh pancreatic and intestinal juices are mixed together, the result is a powerful proteolytic mixture, though neither juice by itself has any proteolytic activity.

Pawlow speaks of the substance in the intestinal juice which has this action as a "ferment of the ferments," and has named it *enterokinase.* It mainly reinforces tryptic activity, but also has a similar though slighter energising influence on the fat-splitting ferment.

Starling, like Pawlow, worked with dogs, and has confirmed his main results. A valuable contribution to the same subject has also been made by Hamburger. He has had the unusual opportunity of examining human succus entericus. It became necessary in a patient for surgical reasons to isolate a loop of the small intestine, and this loop continued to discharge intestinal juice to the exterior for some time after the operation. He finds that this juice, like that of the dog, contains a substance which renders pancreatic juice active. He could not find that it exercised any energising influence on the fat-splitting and amylolytic ferments of the pancreas, but its action on the tryptic ferment was most marked. His quantitative experiments do not bear out Pawlow's view that the active substance in the intestinal juice is a ferment, for it is unable like a ferment to act on an unlimited amount of pancreatic juice. Delezenne also thinks it is not a ferment, but compares it to the immune body or amboceptor which enables hæmolysins to become effective (see p. 443). Starling, however, supports Pawlow's view; provided sufficient time is allowed to elapse, it will energise any amount of pancreatic juice.

Another discovery in connection with succus entericus has been made by Otto Cohnheim. The juice has no action on native proteids like fibrin and egg-white,* but it acts on proteoses and peptone. It rapidly breaks them up into simpler substances of which ammonia, leucine, tyrosine, and the hexone bases have been identified. Cohnheim has named the ferment to which this is due *erepsin.* Hamburger found that erepsin is also present in the human juice; it is not identical with enterokinase because erepsin is destroyed by heating the juice to 59° C. for three hours; enterokinase is not destroyed until the temperature is raised to 67° C. Other observers have confirmed the discovery of erepsin, but have found that it or a similar ferment is present in most tissues; it is most abundant in the kidney (Vernon).

The products of erepsin action are not discoverable in the blood or lymph-stream; they must therefore be resynthesised into proteids during the process of absorption.

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* Cohnheim has investigated the action of erepsin on a large number of proteids: it acts energetically on proteoses, peptone, and protamines: on histone, which occupies an intermediate place between protamines and the proteids proper, it has a slight action. On the proteids proper it has no action, with the single exception of caseinogen, which is speedily broken up into simple substances; this opens up the interesting physiological possibility that the suckling infant is able to digest its proteid nutriment even if pepsin and trypsin are absent.

The **bile**, as we shall find, has little or no digestive action by itself, but combined with pancreatic juice it assists the latter in all its actions. This is true for the digestion of starch and of proteid, but most markedly so for the digestion of fat. Occlusion of the bile-duct by a gall-stone or by inflammation prevents bile entering the duodenum. Under these circumstances the fæces contain a large amount of undigested fat.

The importance of the work of Pawlow, and the other physiologists whose names have been mentioned, arises from the entirely new light thrown upon the digestion process as a whole. We have been too apt to think of the occurrences in the alimentary canal as a series of isolated phenomena. We now see that not only is there a beautiful adjustment in the quantity and composition of the various juices to the kind of work they have to do, but each step follows in an orderly manner as the result of the previous steps. For example, the acid gastric juice reaches the small intestine, and there produces secretin from its forerunner; the secretin is taken by the blood-stream to the pancreas, where it excites a flow of pancreatic juice; this juice arrives in the duodenum ready to act on starchy substances and on fat. With the assistance of the bile fatty acid is liberated which in its turn forms more secretin, and so more pancreatic juice. The pancreatic juice, however, cannot act on proteids without enterokinase, which is supplied by the succus entericus; * this sets free the trypsin; and trypsin effectively carries out digestive proteolysis.

Bacterial Action.

The gastric juice is an antiseptic; the pancreatic juice is not. An alkaline fluid like pancreatic juice is just the most suitable medium for bacteria to flourish in. Even in an artificial digestion the fluid is very soon putrid, unless special precautions to exclude or kill bacteria are taken. It is often difficult to say where pancreatic action ends and bacterial action begins, as many of the bacteria that grow in the intestinal contents (having reached that situation in spite of the gastric juice) act in the same way as the pancreatic juice. Some form sugar from starch, others peptone, leucine, and tyrosine from proteids, while others, again, break up fats. There are, however, certain actions that are entirely due to these putrefactive organisms.

i. On carbohydrates. The most frequent fermentation they set up is the lactic acid fermentation: this may go further and result in the formation of carbonic acid, hydrogen, and butyric acid (see p. 391). Cellulose is broken up into carbonic acid and methane. This is the chief cause of the gases in the intestine, the amount of which is increased by vegetable food.

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* The mixture of pancreatic and intestinal juice is extraordinarily powerful. If secretin is administered to a fasting animal the juice secreted, having no food to act upon, will produce erosion and inflammation of the intestinal wall. (Starling.)

ii. On fats. In addition to acting like steapsin, they produce lower acids (valeric, butyric, etc.). The formation of acid products from fats and carbohydrates gives to the intestinal contents an acid reaction. Recent researches show that the contents of the intestine become acid much higher up than was formerly supposed. Organic acids do not, however, hinder pancreatic digestion.

iii. On proteids. Fatty acids and amino-acids, especially leucine and tyrosine, are produced; but these putrefactive organisms have a special action in addition, producing substances having an evil odour, like indole (C_8H_7N), skatole (C_9H_9N), and phenol (C_6H_6O). There are also gaseous products in some cases.

If excessive, putrefactive processes are harmful; if within normal limits, they are useful, helping the pancreatic juice, and, further, preventing the entrance into the body of poisonous products. It is possible that, in digestion, poisonous alkaloids are formed. Certainly this is so in one well-known case. Lecithin, a material contained in small quantities in many foods, and in large quantities in egg-yolk and brain, is broken up by the pancreatic juice into glycerin, phosphoric acid, fatty acid, and an alkaloid called choline. We are, however, protected from the poisonous action of choline by the bacteria, which break it up into carbonic acid, methane, and ammonia.

Leucine and Tyrosine.

These two substances have been frequently mentioned in the preceding pages. They are important as types of the simpler decomposition products of proteids.

They belong to the group of amino-acids. On p. 393 we have given a list of the fatty acids; if we replace one of the hydrogen atoms in a fatty acid by the amino-group (NH_2), we obtain what is called an amino-acid. Take acetic acid: its formula is $CH_3.COOH$; replace one H by NH_2, and we get $CH_2.NH_2.COOH$, which is *amino-acetic acid*, or *glycine*. If we take caproic acid—a term a little higher in the series—its formula is $C_5H_{11}.COOH$; amino-caproic acid is $C_5H_{10}.NH_2.COOH$, which is also called **leucine**.

According to the way in which the amino-group is linked, a large number of isomeric amino-caproic acids, all with the same empirical formula, are theoretically possible. Some of these have been actually prepared in the laboratory; and chemical research has shown that the amino-caproic acid called leucine formed during digestion should be more accurately named *a*-amino-isobutylacetic acid $(CH_3)_2CH.CH_2.CH(NH_2)COOH$.

Tyrosine is a little more complicated, as it is not only an amino-acid, but also contains an aromatic radicle. Propionic acid has the formula $C_2H_5.COOH$; amino-propionic acid is $C_2H_4.NH_2.COOH$, and is called *alanine*. If another H in this is replaced by oxyphenyl $(C_6H_4.OH)$, we get $C_2H_3.NH_2.C_6H_4OH.COOH$, which is oxyphenyl-amino-propionic acid, or tyrosine. Leucine and tyrosine are both crystalline; the former crystallises in the form of spheroidal clumps of crystals, the latter in collections of fine silken needles (fig. 400).

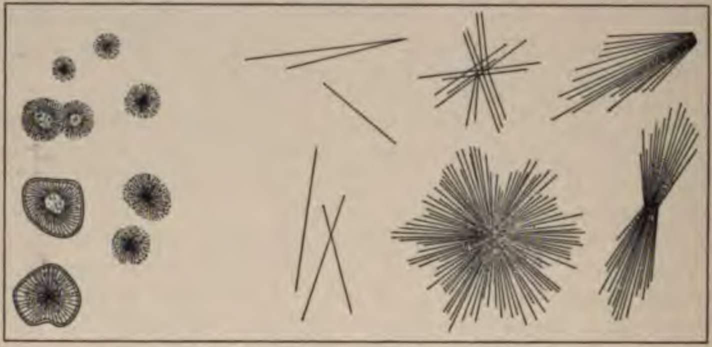

FIG. 400.—Crystals of leucine and tyrosine. × 216.

Polypeptides.—E. Fischer has shown that in the cleavage of the proteid molecule an intermediate stage in the formation of individual animo-acids is that of the polypeptides, which are conjugated groups of such acids. Thus, he has separated out, among others, leucyl-leucine, glycyl-leucine, glycyl-asparagine, alanyl-glycyl-leucine. He has also succeeded in making some of these synthetically, and so there is some promise in the future of a synthesis of the proteid molecule itself.

Extirpation of the Pancreas.

Complete removal of the pancreas in animals and diseases of the pancreas in man produce a condition of diabetes, in addition to the loss of pancreatic action in the intestines. Grafting the pancreas from another animal into the abdomen of the animal from which the pancreas has been removed relieves the diabetic condition.

How the pancreas acts other than in producing the pancreatic juice is not known. It must, however, have other functions related to the general metabolic phenomena of the body, which are disturbed by removal or disease of the gland. This is an illustration of a universal truth—viz., that each part of the body does not merely do its own special work, but is concerned in the great cycle of changes which is called general metabolism. Interference with any organ upsets not only its specific function, but causes disturbances through the body generally. The interdependence of the circulatory and respiratory systems is a well-known instance. Removal of the thyroid gland upsets the whole body, producing widespread changes known as myxœdema. Removal of the testis produces not only a loss of the spermatic secretion, but changes the whole growth and appearance of the animal. Removal of the greater part of the kidneys produces rapid wasting and the breaking down of the tissues to form an increased quantity of urea. The precise way in which these glands are related to the general body processes is, however, a subject of which we know as yet very little. The theory at present most in favour is that certain glands produce an *internal secretion*, which leaves them *viâ* the lymph, and is then distributed to minister to parts elsewhere. The question of the internal secretions of the thyroid and suprarenal capsules is discussed in Chap. XXIII. In the case of the pancreas, Schäfer has propounded the theory that its internal secretion, stoppage of which in some way leads to diabetes, is produced in the islets of epithelium-like cells scattered through the connective tissue of the organ (see fig. 398, p. 491).

Doubt is cast upon the above hypothesis concerning the function of these "islets of Langerhans" by some recent work of Dale's. He showed that the number of islets increases with activity; he regards them as phases in the life history of the secreting cells, and considers that they represent a stage of extreme exhaustion of these cells. In the fœtal pancreas, all the cells have the appearance of islet cells, and so it is probable that in the adult the islets recover their properties, and an alveolar arrangement, and with this their secretory activity.

Adaptation of the Pancreas.—On p. 494 some instances are given of the power of the pancreas to adapt its secretion to the needs of digestion. Bainbridge has shown that in certain cases this is done by a chemical messenger; the pancreatic juice of a dog normally contains no ferment (lactase) capable of hydrolysing milk-sugar into dextrose and galactose, but a dog fed for some time on milk has lactase in its pancreatic juice. This is due to the milk-sugar acting on the intestinal mucous membrane in such a way as to produce some chemical material, which is taken by the blood to the pancreas, where it excites the secretion of this unusual enzyme; for if one injects an extract of the intestinal membrane of a milk-fed dog into a normal dog, the latter animal immediately secretes lactase in its pancreatic juice.

CHAPTER XXXIII

THE LIVER

THE **Liver**, the largest gland in the body, situated in the abdomen on the right side chiefly, is an extremely vascular organ, and receives its supply of blood from two distinct sources, viz., from the *portal vein* and from the *hepatic artery*, while the blood is returned from it into the vena cava inferior by the *hepatic veins*. Its secretion, the *bile*, is conveyed from it by the *hepatic duct*, either directly into the intestine, or, when digestion is not going on, into the *cystic* duct, and thence into the gall-bladder, where it accumulates until required. The portal vein, hepatic artery, and hepatic duct branch together throughout the liver, while the hepatic veins and their tributaries run by themselves.

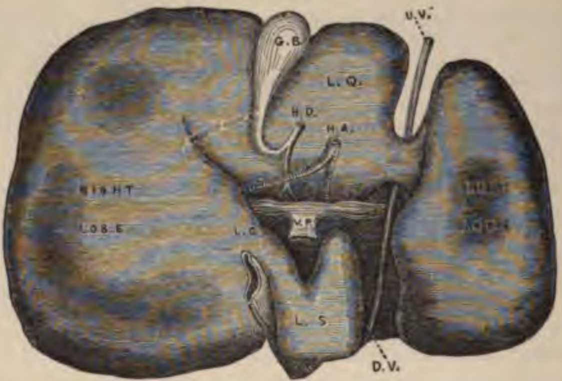

FIG. 401.—The under surface of the liver. G. B., gall-bladder; H. D., common bile-duct; H. A., hepatic artery; V. P., portal vein; L. Q., lobulus quadratus; L. S., lobulus spigelii; L. C., lobulus caudatus; D. V., ductus venosus; U. V., umbilical vein. (Noble Smith.)

On the outside, the liver has an incomplete covering of peritoneum, and beneath this is a very fine coat of areolar tissue, continuous over the whole surface of the organ. It is thickest where the peritoneum is absent, and is continuous on the general surface of the liver with the fine and, in the human subject, almost imperceptible areolar tissue investing the lobules. At the transverse fissure it is merged in the areolar investment called Glisson's capsule, which, surrounding the portal vein, hepatic artery and hepatic duct, accompanies them in their branchings through the substance of the liver.

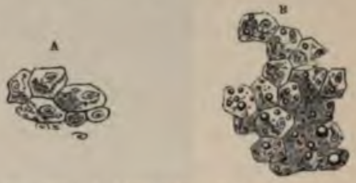

FIG. 402.—A. Liver-cells. B. Ditto, containing various-sized particles of fat.

Structure.—The liver is in origin a tubular gland, but as development progresses it soon loses all resemblance to the tubular glands found elsewhere. It is made up of small roundish or oval portions called *lobules*, each of which is about $\frac{1}{20}$ of an inch (about 1 mm.) in diameter, and composed of the liver cells, between which the blood-vessels and bile-vessels ramify. The *hepatic cells* (fig. 406), which form the glandular or secreting part of the liver, are of a spheroidal form, somewhat polygonal from mutual pressure, about $\frac{1}{800}$ to $\frac{1}{1000}$ inch (about $\frac{1}{32}$ to $\frac{1}{40}$ mm.) in diameter, possessing a nucleus, sometimes two. The cell-substance, composed of protoplasm, contains numerous fatty particles, as well as a variable amount of glycogen. The cells sometimes exhibit slow amœboid movements. They are held together by a very delicate sustentacular tissue, continuous with the inter-lobular connective tissue.

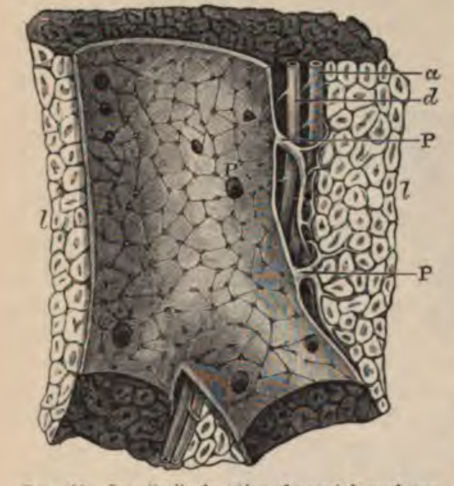

FIG. 403.—Longitudinal section of a portal canal, containing a portal vein, hepatic artery and hepatic duct, from the pig. P, branch of vena portæ, situated in a portal canal amongst the lobules of the liver; *l*, *l*, and giving off vaginal branches; there are also seen within the large portal vein numerous orifices of the smallest interlobular veins arising directly from it; *a*, hepatic artery; *d*, bile duct. × 5. (Kiernan.)

To understand the distribution of the blood-vessels in the liver, it will be well to trace, first, the two blood-vessels and the duct which enter the organ on the under surface at the transverse fissure, viz., the portal vein, hepatic artery, and hepatic duct. As before remarked, all three run in company, and their appearance on longitudinal section is shown in fig. 403. Running together

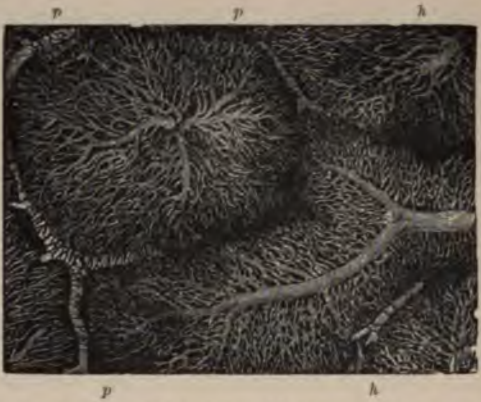

FIG. 404.—Capillary network of the lobules of the rabbit's liver. The figure is taken from a very successful injection of the liver veins, made by Harting: it shows nearly the whole of two lobules, and parts of three others; *p*, interlobular (portal) branches running in the interlobular spaces; *h*, intralobular (hepatic) veins occupying the centre of the lobules. The interlobular and intralobular vessels are connected by radiating capillaries. × 45. (Kölliker.)

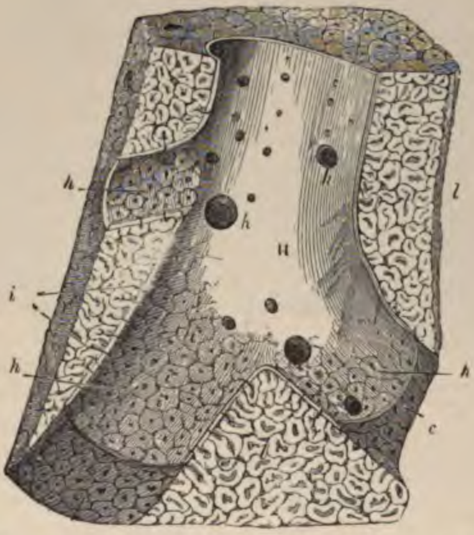

FIG. 405.—Section of a portion of liver passing longitudinally through a considerable hepatic vein, from the pig. H, hepatic venous trunk, against which the sides of the lobules (*l*) are applied; *h*, *h*, *h*, sublobular hepatic veins, on which the bases of the lobules rest, and through the coats of which they are seen as polygonal figures; *i*, mouth of the intralobular veins, opening into the sublobular veins; *i'*, intralobular veins shown passing up the centre of some divided lobules; *l*, *l*, cut surface of the liver; *c*, *c*, walls of the hepatic venous canal, formed by the polygonal bases of the lobules. × 5. (Kiernan.)

through the substance of the liver, they are contained in small channels called *portal canals*, their immediate investment being a sheath of areolar tissue continuous with Glisson's capsule.

To take the distribution of the portal vein first:—In its course through the liver this vessel gives off small branches which divide and subdivide *between* the lobules surrounding them and limiting them, and from this circumstance called *inter*-lobular veins. From these vessels a dense capillary network is prolonged into the substance of the lobule, and this network converges to a single small vein, occupying the centre of the lobule, and hence called *intra*-lobular. This arrangement is well seen in fig. 404, which represents a section of a small piece of an injected liver.

The small *intra*-lobular veins discharge their contents into veins called *sub*-lobular (*h h h*, fig. 405); while these, again, by their union, form the main branches of the *hepatic* veins, which leave the posterior border of the liver to end by two or three principal trunks in the inferior vena cava, just before its passage through the diaphragm. The *sub-lobular* and *hepatic veins*, unlike the *portal* vein and its companions, have little or no areolar tissue around them, and their coats are very thin.

The hepatic artery, the chief function of which is to distribute blood for nutrition to Glisson's capsule, the walls of the ducts and blood-vessels, and other parts of the liver, is distributed in a very similar manner to the portal vein, its blood being returned by small branches which pass into the capillary plexus of the lobules which connects the *inter*- and *intra*-lobular veins.

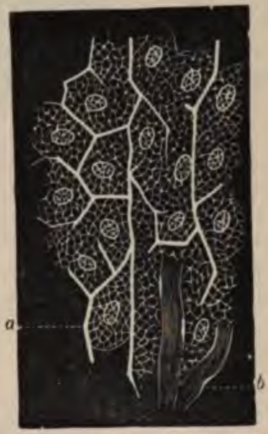

Fig. 406.—Portion of a lobule of liver. *a*, bile capillaries between liver-cells, the network in which is well seen; *b*, blood capillaries. × 350. (Klein and Noble Smith.)

The hepatic duct divides and subdivides in a manner very like that of the portal vein and hepatic artery, the larger branches being lined by *columnar*, and the smaller by small *polygonal* epithelium.

The bile-capillaries commence between the hepatic cells, and are bounded by a delicate membranous wall of their own. They are always bounded by hepatic cells on all sides, and are thus separated from the nearest blood-capillary by at least the breadth of one cell (figs. 406 and 407).

To demonstrate the intercellular network of bile capillaries, Chrzonszezewsky employed a method of natural injection. A saturated aqueous solution of sulph-indigotate of soda is introduced into the circulation of dogs and pigs by the jugular vein. The animals are killed an hour and a half afterwards, and the blood-vessels washed free from blood, or injected with gelatin stained with carmine. The bile-ducts are then seen filled with blue, and the blood-vessels with red material. If the animals are killed sooner than this, the pigment is found within the hepatic cells, thus demonstrating it was through their agency that the canals were filled.

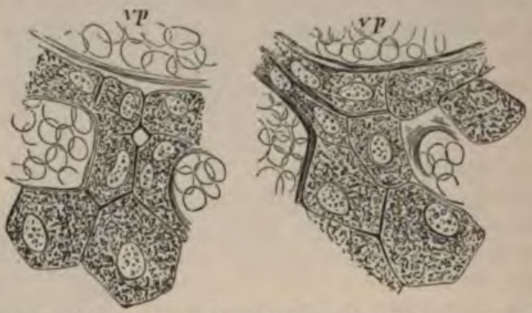

FIG. 407.—Hepatic cells and bile capillaries, from the liver of a child three months old. Both figures represent fragments of a section carried through the periphery of a lobule. The red corpuscles of the blood are recognised by their circular contour; *vp*, corresponds to an interlobular vein in immediate proximity with which are the epithelial cells of the biliary ducts, to which, at the lower part of the figures, the much larger hepatic cells suddenly succeed. (E. Hering.)

Pflüger and Kupffer have since this shown that the relation between the hepatic cells and the bile-canaliculi is even more intimate, for they have demonstrated the existence of vacuoles in the cells communicating by minute intracellular channels with the adjoining bile-canaliculi (fig. 408). It is important to notice that the

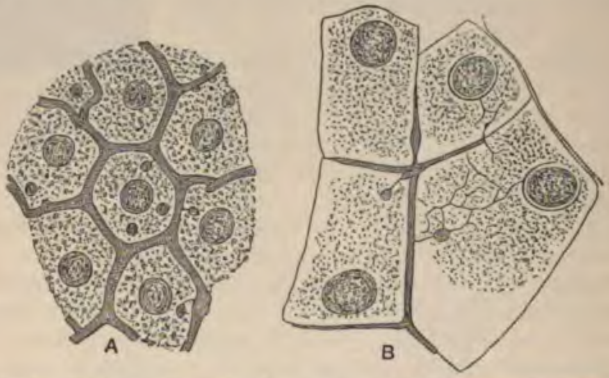

FIG. 408.—Sketches illustrating the mode of commencement of the bile-canaliculi within the liver-cells (Heidenhain, after Kupffer). A, rabbit's liver, injected from hepatic duct with Berlin blue. The intercellular canaliculi give off minute twigs which penetrate into the liver-cells, and there terminate in vacuole-like enlargements. B, frog's liver naturally injected with sulph-indigotate of soda. A similar appearance is obtained, but the communicating twigs are ramified.

bile-canaliculi are always separated by at least a portion of a cell from the nearest blood-capillaries, and that the formation of bile is no mere transudation from the blood or lymph. The liver-cells take certain materials from the plasma and elaborate the constituents of the bile, the bile-salts and the bile pigments. There can be no doubt that these substances are formed by the hepatic cells, for they are not found in the blood nor in any other organ or tissue; and after extirpation of the liver they do not accumulate in the blood.

Intracellular canaliculi in the liver-cells are not unique. Recent research by Golgi's method has shown that in the salivary and gastric glands, and in the pancreas, there is a similar condition of affairs.

Schäfer states that the liver-cells contain not only the intracellular bile-canaliculi, but also intracellular blood-canaliculi passing off from the capillaries between the cells. These are too minute to admit blood-corpuscles.

The **Gall-bladder** (G. B., fig. 401) is a pyriform bag, attached to the under surface of the liver, and supported also by the peritoneum, which passes below it. The larger end, or *fundus*, projects beyond the front margin of the liver; while the smaller end contracts into the cystic duct. Its wall is constructed of three coats. (1) Externally (excepting that part which is in contact with the liver) is the *serous* coat, which has the same structure as the peritoneum with which it is continuous. Within this is (2) the *fibrous* or areolar coat, with which is mingled a considerable number of plain muscular fibres, both longitudinal and circular. (3) Internally the gall-bladder is lined by mucous membrane and a layer of columnar epithelium. The surface of the mucous membrane presents to the naked eye a minutely honeycombed appearance from a number of tiny polygonal depressions with intervening ridges, by which its surface is mapped out. In the cystic duct the mucous membrane is raised up in the form of crescentic folds, which together appear like a spiral valve, and which assist the gall-bladder in retaining the bile during the intervals of digestion.

The gall-bladder and all the main biliary ducts are provided with mucous glands, which open on the internal surface.

Functions of the Liver.

The functions of the liver are connected with the general metabolism of the body, especially in connection with the metabolism of carbohydrates (glycogenic function); and in connection with the metabolism of nitrogenous material (formation of urea and uric acid). This second function we shall discuss with the urine. The third function is the formation of bile, which must very largely be regarded as a subsidiary one, bile containing the waste products of the liver, the results of its other activities. This, however, it will be convenient to take first.

Bile.

Bile is the secretion of the liver which is poured into the duodenum: it has been collected in living animals by means of a biliary fistula; the same operation has occasionally been performed in human beings. After death the gall-bladder yields a good supply of bile which is more concentrated than that obtained from a fistula.

Bile is being continuously poured into the intestine, but there is an increased discharge immediately on the arrival of food in the duodenum; there is a second increase in secretion a few hours later.

Though the chief blood supply of the liver is by a vein (the portal vein), the amount of blood in the liver varies with its needs, being increased during the periods of digestion. This is due to the fact that in the area from which the portal vein collects blood—stomach, intestine, spleen, and pancreas — the arterioles are all dilated, and the capillaries are thus gorged with blood. Further, the active peristalsis of the intestine and the pumping action of the spleen are additional factors in driving more blood onwards to the liver.

The bile being secreted from the portal blood is secreted at much lower pressure than one finds in glands such as the salivary glands, the blood supply of which is arterial. Heidenhain found that the pressure in the bile duct of the dog averages 15 mm. of mercury, which is nearly double that in the portal vein. This fact is of considerable importance, as it illustrates the general truth that secretion is not mere process of passive filtration, but that the cells exercise secretory force.

The second increase in the flow of bile—that which occurs some hours after the arrival of the semi-digested food (chyme) in the intestine—appears to be due to the effect of the digestive products carried by the blood to the liver, stimulating the hepatic cells to activity: this is supported by the fact that proteid food increases the quantity of bile secreted, whereas fatty food which is absorbed, not by the portal vein, but by the lacteals, has no such effect.

The chemical process by which the constituents of the bile are formed is obscure. We, however, know that the biliary pigment is produced by the decomposition of hæmoglobin. Bilirubin is, in fact, identical with the iron-free derivative of hæmoglobin called hæmatoidin, which is found in the form of crystals in old blood-clots such as occur in the brain after cerebral hæmorrhage (see p. 431).

An injection of hæmoglobin into the portal vein or of substances like water which liberate hæmoglobin from the red blood-corpuscles produces an increase of bile pigment. If the spleen takes any part in the elaboration of bile pigment, it does not proceed so far as to liberate hæmoglobin from the corpuscles. No free hæmoglobin is discoverable in the blood plasma in the splenic vein.

The amount of bile secreted is differently estimated by different observers; the amount secreted daily in man varies from 500 c.c. to a litre (1000 c.c.).

The constituents of the bile are the bile salts proper (taurocholate and glycocholate of soda), the bile pigments (bilirubin, biliverdin), a mucinoid substance, small quantities of fats, soaps, cholesterin, lecithin, urea, and mineral salts, of which sodium chloride and the phosphates of iron, calcium, and magnesium are the most important.

Bile is a yellowish, reddish-brown, or green fluid, according to the relative preponderance of its two chief pigments. It has a musk-like odour, a bitter-sweet taste, and a neutral or faintly alkaline reaction.

The specific gravity of human bile from the gall-bladder is 1026 to 1032; that from a fistula, 1010 to 1011. The greater concentration of gall-bladder bile is partly but not wholly explained by the addition to it from the walls of that cavity of the mucinoid material it secretes.

The amount of solids in bladder bile is from 9 to 14 per cent., in fistula bile from 1·5 to 3 per cent. The following table shows that this low percentage of solids is almost entirely due to want of bile salts. This can be accounted for in the way first suggested by Schiff—that there is normally a bile circulation going on in the body, a large quantity of the bile salts that pass into the intestine being first split up, then reabsorbed and again secreted. Such a circulation would obviously be impossible in cases where all the bile is discharged to the exterior.

The following table gives some important analyses of human bile:—

Constituents.	Fistula bile (healthy woman. Copeman and Winston).	Fistula bile (case of cancer. Yeo and Herroun).	Normal bile (Frerichs).
Sodium glycocholate .	0·6280	0·165	9·14
Sodium taurocholate .		0·055	
Cholesterin, lecithin, fat .	0·0990	0·038	1·18
Mucinoid material . .	0·1725	0·148	2·98
Pigment	0·0725		
Inorganic salts . .	0·4510	0·878	0·78
Total solids . . .	1·4230	1·284	14·08
Water (by difference) .	98·5570	98·716	85·92
	100·0000	100·000	100·00

Bile Mucin.—There has been considerable diversity of opinion as to whether bile mucin is really mucin. The most recent work in Hammarsten's laboratory shows that differences occur in different animals. Thus in the ox there is very little true mucin, but a great amount of nucleo-proteid; in human bile, on the other hand, there is very little if any nucleo-proteid; the mucinoid material present there is really mucin.

The Bile Salts.—The bile contains the sodium salts of complex amino-acids called the bile acids. The two acids most frequently found are glycocholic and taurocholic acids. The former is the more abundant in the bile of man and herbivora; the latter in carnivorous animals, like the dog. The most important difference between the two acids is that taurocholic acid contains sulphur, and glycocholic acid does not.

Glycocholic acid ($C_{26}H_{43}NO_6$) is by the action of dilute acids and alkalis, and also in the intestine, hydrolysed and split into glycine or amino-acetic acid and cholalic acid.

$$\underset{\text{[Glycocholic acid.]}}{C_{26}H_{43}NO_6} + H_2O = \underset{\text{[Glycine.]}}{C_2H_5NO_2} + \underset{\text{[Cholalic acid.]}}{C_{24}H_{40}O_5}.$$

The glycocholate of soda has the formula $C_{26}H_{42}NaNO_6$.

Taurocholic acid ($C_{26}H_{45}NO_7S$) similarly splits into taurine or amino-isethionic acid and cholalic acid.

$$\underset{\text{[Taurocholic acid.]}}{C_{26}H_{45}NO_7S} + H_2O = \underset{\text{[Taurine.]}}{C_2H_7NO_3S} + \underset{\text{[Cholalic acid.]}}{C_{24}H_{40}O_5}$$

The taurocholate of soda has the formula $C_{26}H_{44}NaNO_7S$.

The colour reaction called **Pettenkofer's reaction**, is due to the presence of cholalic acid. Small quantities of cane sugar and strong sulphuric acid are added to the bile. The sulphuric acid acting on sugar forms a small quantity of a substance called *furfuraldehyde*, in addition to other products. The furfuraldehyde gives a brilliant purple colour with cholalic acid.

The Bile Pigments.—The two chief bile pigments are bilirubin and biliverdin. Bile which contains chiefly the former (such as dog's bile) is of a golden or orange-yellow colour, while the bile of many herbivora, which contains chiefly biliverdin, is either green or bluish-green. Human bile is generally described as containing chiefly bilirubin, but there have been some cases described in which biliverdin was in excess. The bile pigments show no absorption bands with the spectroscope; their origin from the blood pigment has already been stated.

Bilirubin has the formula $C_{16}H_{18}N_2O_3$: it is thus an iron-free derivative of hæmoglobin. The iron is apparently stored up in the liver cells, perhaps for future use in the manufacture of new hæmoglobin. The bile contains only a trace of iron.

Biliverdin has the formula $C_{16}H_{18}N_2O_4$ (*i.e.*, one atom of oxygen more than in bilirubin): it may occur as such in bile; it may be formed by simply exposing red bile to the oxidising action of the atmosphere; or it may be formed as in Gmelin's test by the more vigorous oxidation produced by fuming nitric acid.

Gmelin's test consists in a play of colours—green, blue, red, and finally yellow, produced by the oxidising action of fuming nitric acid (that is, nitric acid containing nitrous acid in solution). The end or yellow product is called *choletelin*, $C_{16}H_{18}N_2O_6$.

Hydrobilirubin.—If a solution of bilirubin or biliverdin in dilute alkali is treated with sodium amalgam or allowed to putrefy, a brownish pigment, which is a reduction product, is formed called hydrobilirubin, $C_{32}H_{40}N_4O_7$. With the spectroscope it shows a dark absorption band between *b* and F, and a fainter band in the region of the D line.

This substance is interesting because a similar substance is formed from the bile pigment by reduction processes in the intestine, and constitutes *stercobilin*, the pigment of the fæces. Some of this is absorbed and ultimately leaves the body in the urine as one of its pigments called *urobilin*. A small quantity of urobilin is sometimes found preformed in the bile. The identity of urobilin and stercobilin has been frequently disputed, but the recent work of Garrod and Hopkins has confirmed the old statement that they are the same substance with different names. Hydrobilirubin differs from urobilin in containing more nitrogen in its molecule (9·2 instead of 4·1 per cent.).

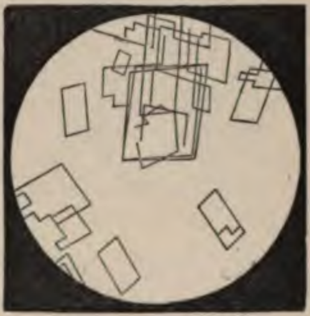
FIG. 409.—Crystalline scales of cholesterin.

Cholesterin.—This substance is contained not only in bile, but very largely in nervous tissues. Like lecithin, it is an abundant constituent of the white substance of Schwann. It is found also in blood-corpuscles. In bile it is normally present in small quantities only, but it may occur in excess, and form the concretions known as gall-stones, which are usually more or less tinged with bilirubin.

Though its solubilities remind one of a fat, cholesterin is not a fat. It is, in fact, chemically speaking, a monatomic alcohol. Its formula is $C_{27}H_{45}.HO$.

From alcohol or ether containing water it crystallises in the form of rhombic tables, which contain one molecule of water of crystallisation: these are easily recognised under the microscope (see fig. 409).

It gives the following colour tests:—

1. Heated with sulphuric acid and water (5 : 1), the edges of the crystals turn red.

2. A solution of cholesterin in chloroform, shaken with an equal amount of concentrated sulphuric acid, turns red, and ultimately purple, the subjacent acid acquiring a green fluorescence. (Salkowski's reaction.)

"The mode of origin of cholesterin in the body has not been clearly made out. Whether it is formed in the tissues generally, in the blood, or in the liver, is not known; nor has it been determined conclusively that it is derived from albuminous or nervous matter. It is also doubtful if we are to regard it as a waste substance of no use to the body, as its presence in the blood-corpuscles, in nervous matter, in the egg, and in vegetable grains, points to a possible function of a histogenetic or tissue-forming character." (McKendrick.)

A substance called *iso-cholesterin*, isomeric with ordinary cholesterin, is found in the fatty secretion of the skin (sebum); it is largely contained in the preparation called *lanoline* made from sheep's-wool fat. It does not give Salkowski's reaction with chloroform and sulphuric acid just described.

The Uses of Bile.—Bile is doubtless, to a large extent, excretory. Some state that it has a slight action on fats and carbohydrates, but its principal action is as a coadjutor to the pancreatic juice (especially in the digestion of fat). In some animals it has a feeble diastatic power.

Bile is said to be a natural antiseptic, lessening the putrefactive processes in the intestine. This is very doubtful. Though the bile salts are weak antiseptics, the bile itself is readily putrescible, and the power it has of diminishing putrescence in the intestine is due chiefly to the fact that by increasing absorption it lessens the amount of putrescible matter in the bowel.

When the bile meets the chyme the turbidity of the latter is increased owing to the precipitation of unpeptonised proteid. This is an action due to the bile salts, and it has been surmised that this conversion of the chyme into a more viscid mass is to hinder somewhat its progress through the intestines; it clings to the intestinal wall, thus allowing absorption to take place.

Bile is alkaline; it therefore assists the pancreatic juice in neutralising the acid mixture that leaves the stomach.

Bile assists the absorption of fats, as we shall see in studying that subject. It is also a solvent of fatty acids.

We have seen that fistula bile is poor in solids as compared with normal bile, and that this is explained on the supposition that the normal bile circulation is not occurring—the liver cannot excrete what it does not receive back from the intestine. Schiff was the first to show that if the bile is led back into the duodenum, or even if the animal is fed on bile, the percentage of solids in the bile excreted is at once raised. It is on these experiments that the theory of a bile circulation is mainly founded. The bile circulation relates, however, chiefly, if not entirely, to the bile salts: they are found but sparingly in the fæces; they are only represented to a slight extent in the urine: hence it is calculated that seven-eighths of them are re-absorbed from the intestine. Small quantities of cholalic acid, taurine, and glycine are found in the fæces; the greater part of these products of the decomposition of the bile salts is taken by the portal vein to the liver, where they are once more synthesised into the bile salts. Some of the taurine is absorbed and excreted as tauro-carbamic acid in the urine. Some of the absorbed glycine may be excreted as urea or uric acid. The cholesterin and mucus are found in the fæces; the pigment is changed into stercobilin (see p. 511).

The bile-expelling mechanism must be carefully distinguished from the bile-secreting action of the liver-cells. The bile is forced into the ducts, and ultimately into the duodenum, by the pressure of newly-formed bile pressing on that previously in the ducts, and this is assisted by the contraction of the plain muscular fibres of the larger ducts and gall-bladder, which occurs reflexly when the food enters the duodenum. In cases of obstruction, as by a gall-stone, in the ducts, this action becomes excessive, and gives rise to the intense pain known as *hepatic colic.*

Many so-called *cholagogues* (bile-drivers), like calomel, act on the bile-expelling mechanism and increase the peristalsis of the muscular tissue; they do not really cause an increased formation of bile.

Jaundice.—The commonest form of jaundice is produced by obstruction in the bile ducts preventing the bile entering the intestine. A very small amount of obstruction, for instance, a plug of mucus produced in excess owing to inflammatory processes, will often be sufficient, as the bile is secreted at such low pressure. Under these circumstances, the fæces are whitish or clay coloured, and the bile passing backwards into the lymph,* enters the blood and is thus distributed over the body, causing a yellow tint in the skin and mucous membranes, and colouring the urine deeply.

In some cases of jaundice, however (*e.g.*, produced by various poisons), there is no obvious obstruction; the causes of non-obstructive, or blood-jaundice, form a pathological problem of some interest. A few years ago it was believed that the bile pigment was actually produced in the blood. But all recent work shows that the liver is the only place where production of bile occurs, and that in all cases of so-called non-obstructive jaundice, the bile is absorbed from the liver. There may be obstruction present in the smaller ducts, or the functions of the liver may be so upset that the bile passes into the lymph even when there is no obstruction.

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* The absorption is by the lymph, because if jaundice is produced in an animal by ligature of the bile duct, it will cease when the thoracic duct is tied.

The Glycogenic Function of the Liver.

The important fact that the liver normally forms sugar, or a substance readily convertible into it, was discovered by Claude Bernard in the following way: he fed a dog for seven days with food containing a large quantity of sugar and starch; and, as might be expected, found sugar in both the portal and hepatic blood. But when this dog was fed with meat only, to his surprise, sugar was still found in the blood of the hepatic veins. Repeated experiments gave invariably the same result; no sugar was found, under a meat diet, in the portal vein, if care were taken, by applying a ligature on it at the transverse fissure, to prevent reflux of blood from the hepatic venous system. Bernard found sugar also in the substance of the liver. It thus seemed certain that the liver formed sugar, even when, from the absence of saccharine and amyloid matters in the food, none could have been brought directly to it from the stomach or intestines.

Bernard found, subsequently, that a liver, removed from the body, and from which all sugar had been completely washed away by injecting a stream of water through its blood-vessels, contained sugar in abundance after the lapse of a few hours. This post-mortem production of sugar was a fact which could only be explained on the supposition that the liver contained a substance readily convertible into sugar; and this theory was proved to be correct by the discovery of a substance in the liver allied to starch, and now termed *glycogen* or animal starch.

We are thus led to the conclusion that glycogen is formed first and stored in the liver cells, and that the sugar, when present, is the result of its transformation.

Source of Glycogen.—Although the greatest amount of glycogen is produced by the liver upon a diet of starch or sugar, a certain quantity is produced upon a proteid diet. It must, then, be produced by protoplasmic activity within the cells. The glycogen when stored in the liver cells may readily be demonstrated in sections of liver containing it by its reaction (red or port-wine colour) with iodine, and moreover, when the hardened sections are soaked in water in order to dissolve out the glycogen, the protoplasm of the cell is so vacuolated as to appear little more than a framework. In the liver of a hibernating frog the amount of glycogen stored up in the outer parts of the liver cells is very considerable.

Average Amount of Glycogen in the Liver of Dogs under various Diets (Pavy).

Diet.	Amount of Glycogen in Liver.
Animal food	7·19 per cent.
Animal food with sugar (about ¼-lb of sugar daily)	14·5 ,,
Vegetable diet (potatoes, with bread or barley-meal)	17·23 ,,

The dependence of the formation of glycogen on the kind of food taken is also well shown by the following results, obtained by the same experimenter:—

Average Quantity of Glycogen found in the Liver of Rabbits after Fasting, and after a Diet of Starch and Sugar respectively.

	Average amount of Glycogen in Liver.
After fasting for three days	Practically absent.
,, diet of starch and grape-sugar	15·4 per cent.
,, ,, cane-sugar	16·9 ,,

The diet most favourable to the production of a large amount of glycogen is a mixed diet containing a large amount of carbohydrate, but with some proteid. Fats taken in as food do not increase the amount of glycogen in the cells. Glycerin injected into the alimentary canal may increase the glycogen of the liver, probably because it hinders the conversion of glycogen into sugar; the glycogen therefore is allowed to accumulate in the liver.

Destination of Glycogen.—There are two chief theories as to the destination of hepatic glycogen. (1.) That the glycogen is converted into sugar during life by the agency of a ferment (*liver diastase*) also formed in the liver; and that the sugar is conveyed away by the blood of the hepatic veins, to undergo combustion in the tissues. (2.) That the conversion into sugar only occurs after death, and that during life no sugar exists in healthy livers, glycogen not undergoing this transformation.

The first view is that of Claude Bernard, and has been adopted by the majority of physiologists. The second view is that of Pavy: he denies that the liver is a sugar-forming organ, he regards it as a sugar-destroying organ; the sugar is stored as animal starch, but never again leaves the liver as sugar during life. He has been unable to find more sugar in the hepatic blood than in the portal blood. Other observers have found an increase in the sugar of the blood leaving the liver, but the estimation of sugar in a fluid rich in proteids is a matter of great difficulty. Even if the increase is so small as hardly to be detected, it must be remembered that the whole blood of the body passes through the liver about twice a minute, so that a very small increase each time would mount up to a large total.

Pavy further denies that the *post-mortem* formation of sugar from glycogen that occurs in an excised liver is a true picture of what occurs during life, but is due to a ferment which is only formed after death. During life, he regards the glycogen as a source of other substances, like fat and proteid. It is certainly a fact that increase of carbohydrate food leads to the formation of fat in the body and in the liver-cells. In support of the theory that glycogen may also contribute to the formation of proteids, he has shown that many proteids contain a carbohydrate radicle.

The whole question is under keen discussion at present. We may state, however, that the prevalent opinion is that the liver-cells may be able to convert part of the store of glycogen into fat, but that most of the glycogen leaves the liver as sugar (dextrose), so justifying the name (literally, mother substance of sugar) given to it by Bernard.

Diabetes.—In certain disorders of hepatic metabolism, the glycogenic function is upset, and excess of sugar passes into the blood, leaving the body in the urine (*glycosuria*). This may be due to an increased formation of sugar from glycogen, or to a diminished formation of glycogen from the sugar of the portal blood, according as either Bernard's or Pavy's view of the liver function is adopted. In many cases the diabetic condition may be removed by a close attention to diet; starchy and saccharine food must be rigidly abstained from.

In other cases, which are much more serious, diet makes little or no difference. Under these circumstances the sugar must come from the metabolism of the proteid constituents of protoplasm.

The disease *diabetes* is not a single one; the term includes many pathological conditions, which all possess in common the symptom of excess of sugar in the blood and urine.

A diabetic condition may be produced in animals artificially in several ways:—

(1) *By diabetic puncture.*—Claude Bernard was the first to show that injury to the floor of the fourth ventricle in the region of the vaso-motor centre leads to glycosuria. The injury produces a disturbance of the vaso-motor mechanism, but diabetes cannot be regarded as purely vaso-motor in origin. This condition is of interest, because brain disease in man, especially in the region of the bulb, is frequently associated with glycosuria.

(2) *By extirpation of the pancreas.*—(See also p. 500). It is probable that in diabetes, the oxidative powers of the body-cells are lessened. Nevertheless, other diseases in which diminished oxidation occurs are not necessarily accompanied with glycosuria. The difficulty in diabetes probably lies in an impairment of the capacity of the cells of the body to prepare the sugar for oxidation. In this

process the sugar or its derivative glycuronic acid is split into smaller molecules and ultimately into water and carbon dioxide. The close relationship of sugar and glycuronic acid is shown by the following formulæ:—

$$\begin{array}{lcl} \mathrm{COH} & \qquad\qquad & \mathrm{COH} \\ \mathrm{(CHOH)_4} & & \mathrm{(CHOH)_4} \\ \mathrm{CH_2OH} & & \mathrm{COOH} \\ \text{[Dextrose.]} & & \text{[Glycuronic acid.]} \end{array}$$

That is two hydrogen atoms in the CH_2OH group are replaced by one of oxygen. This oxidation is readily brought about in the body, and glycuronic acid is usually found in diabetic urine; but the further oxidation into water and carbon dioxide is a more difficult task, because it involves the disruption of the linkage of the carbon atoms. Perhaps it is here that the internal secretion of the pancreas is effective. This, however, is at present a mere theory, and certainly Lépine's idea that the ferment of the pancreatic internal secretion is one which initiates glycolysis or sugar-splitting *in the blood,* has been abundantly disproved. It may be that the active principle of the pancreatic internal secretion stimulates the glycolytic action of the tissue-cells. It is conceivable that in the other great cause of glycosuria, namely, injury to nervous structures, as in Bernard's puncture experiment, the derangement of the nervous system exerts some unknown influence on the pancreas as well as on the liver.

(3) *By administration of phloridzin.*—Many poisons produce temporary glycosuria, but the most interesting and powerful of these is phloridzin. The diabetes produced is very intense. Phloridzin is a glucoside, but the sugar passed in the urine is too great to be accounted for by the small amount of sugar derivable from the drug. Besides that, phloretin, a derivative of phloridzin, free from sugar, produces the same results.

Phloridzin produces diabetes in starved animals, or in those in which any carbohydrate store must have been got rid of by the previous administration of the same drug. Phloridzin-diabetes is therefore analogous to those intense forms of diabetes in man in which the sugar must be derived from protoplasmic metabolism.

A puzzling feature is the absence of an increase of sugar in the blood; if the phloridzin is directly injected into one renal artery, sugar rapidly appears in the secretion of that kidney; the sugar is formed within the kidney cells from some substance in the blood, but whether that substance is proteid or not is uncertain. The action of the kidney cells in forming sugar has been compared to that of the mammary cells in forming lactose.

Acetonæmia.—Death in diabetic patients is usually preceded by deep coma, or unconsciousness. Some poison must be produced that acts soporifically upon the brain. The breath and urine of these patients smell strongly of acetone; hence the term *acetonæmia.* This apple-like smell should always suggest the possible onset of coma and death, but it is exceedingly doubtful whether acetone (which can certainly be detected in the urine) is the true poison; ethyl-diacetic acid, which accompanies, and is the source of the acetone, was regarded by some as the actual poison, but these substances, when introduced into the circulation artificially, do not cause serious symptoms. The principal poison is amido-hydroxybutyric acid. The alkalinity and carbonic acid of the blood are decreased, and the ammonia of the urine is increased; this indicates an attempt of the body to neutralise the poisonous acids.

The Nerves of the Liver.

Claude Bernard observed that an increase of sugar in the blood is brought about by stimulation of the central and peripheral ends of the divided vagus, and that on the section of both vagi sugar disappears from the blood, and glycogen from the liver and tissues generally. These results have been confirmed in recent experiments, and it has been in addition found that stimulation of the cœliac plexus also leads to a loss of glycogen in the liver, with a corresponding production of glucose that passes into the blood. The disappearance of glycogen from the liver cells after the stimulation of these nerves can also be seen histologically (Cavazzani). These results are due to a direct influence of the nerves on the liver cells, for they are obtained after the circulation is stopped by ligature of the aorta and portal vein (Morat and Dufourt).

Vaso-motor nerves.—The vaso-constrictor fibres for the portal vein leave the spinal cord in the third to the eleventh thoracic nerves inclusive (Bayliss and Starling). The nerves of the hepatic artery are constrictors contained in the splanchnic, and dilators in both splanchnic and vagus.

CHAPTER XXXIV

THE ABSORPTION OF FOOD

FOOD is digested in order that it may be absorbed. It is absorbed in order that it may be assimilated, that is, become an integral part of the living material of the body.

The digested food thus diminishes in quantity as it passes along the alimentary canal, and the fæces contain the undigested or indigestible residue.

In the mouth and œsophagus the thickness of the epithelium and the quick passage of the food through these parts reduce absorption to a minimum. Absorption takes place more rapidly in the stomach: the small intestine with its folds and villi to increase its surface is, however, the great place for absorption; and although the villi are absent from the large intestine, absorption occurs there also, but to a less extent.

Foods such as water and soluble salts like sodium chloride are absorbed unchanged. The organic foods are, however, considerably changed, colloid materials like starch and proteid being converted respectively into the diffusible materials sugar and peptone.

There are two channels of absorption, the blood-vessels (portal capillaries) and the lymphatic vessels or lacteals.

Absorption, however, is no mere physical process of osmosis and filtration. We must also take into account the fact that the cells through which the absorbed substances pass are living, and in virtue of their inherent activity not only select materials for absorption, but also change those substances while in contact with them. These cells are of two kinds—(1) the columnar epithelium that covers the surface; and (2) the lymph cells in the lymphoid tissue beneath. It is now generally accepted that of the two the former, the columnar epithelium, is the more important.

Absorption of Carbohydrates.—Though the sugar formed from starch by ptyalin and amylopsin is maltose, that found in the blood is glucose. Under normal circumstances little, if any, is absorbed by the lacteals. The glucose is formed from the maltose by the succus entericus, aided by the action of the epithelial cells through which it passes. Cane sugar and milk sugar are also converted into glucoses before absorption.

The carbohydrate food which enters the blood as glucose is taken to the liver, and there stored up in the form of glycogen—a reserve store of carbohydrate material for the future needs of the body. Glycogen, however, is found in animals who take no carbohydrate food. It must, then, be formed by the protoplasmic activity of the liver cells from their proteid constituents. The glycogenic function of the liver is discussed in the chapter preceding this. Glucose is the only sugar from which the liver is capable of forming glycogen. If other carbohydrates like cane sugar or lactose are injected into the blood-stream direct, they are unaltered by the liver, and finally leave the body by the urine.

Absorption of Proteids.—A certain amount of soluble proteid is absorbed unchanged. Thus, after taking a large number of eggs, egg albumin is found in the urine. Patients fed *per rectum* derive nourishment from proteid food, though proteolytic ferments are not present in this part of the intestine.

Most proteid, however, is normally absorbed as peptone and proteose or their decomposition products. Peptones and proteoses are absent from the blood under all circumstances, even from the portal blood during the most active digestion. In other words, during absorption the epithelial cells change the products of proteolysis back once more into native proteids (albumin and globulin).

The greater part of the proteid absorbed passes into the blood; a little into the lymph also; but this undergoes the same change.

When peptone (using the word to include the proteoses also) is injected into the blood-stream, poisonous effects are produced, the coagulability of the blood is lessened, the blood-pressure falls, secretion ceases, and in the dog 0·3 gramme of "peptone" per kilogramme of body-weight is sufficient to kill the animal.

The epithelial cells of the alimentary canal thus protect us from those poisonous effects by converting the harmful peptone into the useful albumin.

The whole question of proteid absorption is in a very unsettled state just now. Cohnheim's discovery of erepsin (p. 497) appears to lend support to the view that the peptones are very largely broken up into simpler substances, but the absence of these in the blood-stream shows that the absorptive epithelium is capable of resynthesising them into proteids. Several observers have noted the small amount of peptones obtainable from the intestinal contents; this may be due to the fact that they are so rapidly absorbed, or it may be due to their having been broken up into simpler substances by trypsin and erepsin. On the other hand, there are some observers who hold that the importance of erepsin has been exaggerated, and that the absorptive epithelium can also resynthesise proteids from proteoses and peptone. It is, however, undeniable that the body can be maintained in health and nitrogenous equilibrium by feeding it on the final crystalline products of pancreatic action (Lœwi), and it is probable that the synthesis of the body proteids from these is accomplished mainly by the intestinal epithelium.

Absorption of Fats.—The fats undergo in the intestine two changes: one a physical change (emulsification), the other a chemical change (saponification). The lymphatic vessels are the great channels for fat absorption, and their name *lacteals* is derived from the milk-like appearance of their contents (*chyle*) during the absorption of fat.

The course which the minute fat-globules take may be studied by killing animals at varying periods after a meal of fat, and making osmic acid microscopic preparations of the villi. Figs. 410 and 411 illustrate the appearances observed by Schäfer.

The columnar epithelium cells become first filled with fatty globules of varying size, which are generally larger near the free border. The globules pass down the cells, the larger ones breaking up into smaller ones during the journey; they are then transferred to the amœboid cells of the lymphoid tissue beneath: these ultimately penetrate into the central lacteal, where they either disintegrate or discharge their cargo into the lymph-stream. The globules are by this time divided into immeasurably small ones, the molecular basis of chyle. The chyle enters the blood-stream by the thoracic duct, and after an abundant fatty meal the blood-plasma is quite milky; the fat droplets are so small that they circulate without hindrance through the capillaries. The fat in the blood after a meal is eventually stored up especially in the cells of adipose tissue. It must, however, be borne in mind that the fat of the body is not exclusively derived from the fat of the food, but it may originate also both from proteid and from carbohydrate.

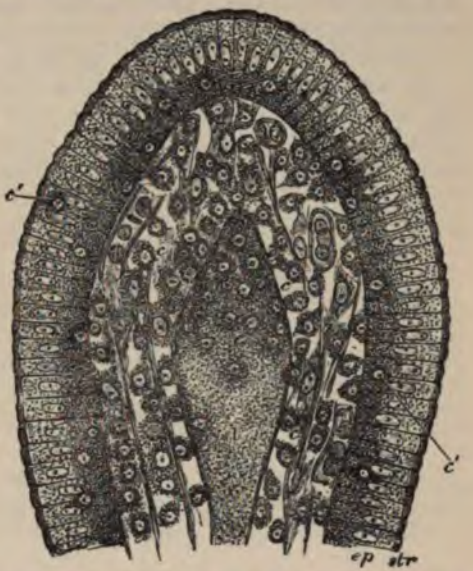

FIG. 410.—Section of the villus of a rat killed during fat absorption. *ep*, epithelium; *str*, striated border; *c*, lymph-cells; *c'*, lymph-cells in the epithelium; *l*, central lacteal containing disintegrating lymph-corpuscles. (E. A. Schäfer.)

The great difficulty in fat absorption was to explain how the fat first gets into the columnar epithelium: these cells will not take up other particles, and it appears certain that the epithelial cells do not in the higher animals protrude pseudopodia from their borders (this, however, does occur in the endoderm of some of the lower invertebrates); moreover, fat particles have never been seen in the striated border of the cells.

Recent research has shown that particles may be present in the epithelium and lymphoid cells while no fat is being absorbed. These particles are apparently protoplasmic in nature, as they stain with reagents that stain protoplasmic granules; they, however, also stain darkly with osmic acid, and so are apt to be mistaken for fat. There is, however, no doubt that the particles found during fat absorption are composed of fat. There is also no doubt that the epithelial cells have the power of forming fat out of the fatty acids and glycerin into which fats have been broken up in the intestine. Munk, who has performed a large number of experiments on the subject, showed that the splitting of fats into glycerin and fatty acids occurs to a much greater extent than was formerly supposed; these substances, being soluble, pass readily into the epithelium cells; and these cells perform the synthetic act of building them into fat once more, the fat so formed appearing in the form of small globules, surrounding or becoming mixed with the protoplasmic granules that are ordinarily present. Another remarkable fact which he made out is that after feeding an animal on fatty acids the chyle contains fat. The necessary glycerin must have been formed by protoplasmic activity during absorption. The more recent work of Moore and Rockwood has shown that fat is absorbed entirely as fatty acid or soap; and that preliminary emulsification, though advantageous for the formation of these substances, is not essential.

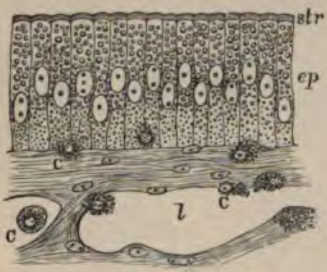

FIG. 411.—Mucous membrane of frog's intestine during fat absorption. *ep*, epithelium; *str*, striated border; C, lymph corpuscles; *l*, lacteal. (E. A. Schäfer.)

We thus see how with increase of knowledge due to improved methods of research, a complete change has come in the ideas physiologists hold regarding this subject. It is not so many years ago, that the physical change—emulsification—which fats undergo in the intestine was considered to be more important than the chemical changes—fat-splitting and saponification. In fact, the small amount of chemical change which was supposed to occur was regarded as quite subordinate, and of value merely in assisting the process of emulsification. We now know that the exact converse is the truth; the chemical change is the important process, and emulsification the subordinate one.

Bile aids the digestion of fat, in virtue of its being a solvent of fatty acids, and it probably assists fat absorption by reducing the surface tension of the intestinal contents; membranes moistened with bile allow fatty materials to pass through them more readily than would otherwise be the case. In cases of disease in which bile is absent from the intestines, a large proportion of the fat in the food passes into the fæces.

Since the days of Lieberkühn it has been the desire of physiologists to prove that the absorption of solutions from the intestines can be explained upon some simple physical basis. Thus the processes of filtration, osmosis, and imbibition, either alone or in combination, have been in turn called upon as affording the requisite explanation. Such theories have alternated with others in which the physical cause has been either wholly or in part rejected as inadequate, and the deficiencies of the physical cause supplemented by the physiological, vital, or selective action of the epithelial lining of the alimentary tract.

The difficulty of the problem does not, however, entirely depend on the impossibility of defining the word vital, but also on the complicated nature of the physical processes to which we have alluded. Since the days when Fischer and Dutrochet inaugurated our elementary knowledge of osmotic phenomena, a great amount of research has been expended in making that knowledge more accurate, but even at the present day it is doubtful whether all the aspects of the question are fully understood (see also p. 321). The subject has, in recent years, been taken up by Waymouth Reid, who has made a life-study of such phenomena, and whose work must be regarded as authoritative.

The animals he experimented on were dogs, and the material selected for absorption was the serum or plasma of the blood from the same animals. The substances to be absorbed were thus of the same kind as those in the blood and lymph on the other side of the absorptive epithelium. The serum or plasma was analysed, introduced into an isolated loop of the gut, and at the end of a given time the contents of the loop were again analysed. The pressure in the loop and in the mesenteric veins was estimated manometrically during the progress of the experiment; allowance was made for the secretion of intestinal juice, and other precautions taken to make each experiment as complete as possible.

It was found that the absorption by an animal of its own serum or plasma takes place under conditions in which filtration or osmosis into blood capillaries or lacteals and also adsorption (or imbibition) are excluded. The active force must therefore by a process of exclusion reside in the physiological activity of the lining epithelium. The same conclusion was reached by another method, namely, that when the epithelium is removed, injured or poisoned, the absorption either ceases or is markedly lessened, and this in spite of the fact that removal of the epithelium must increase the facilities for osmosis and filtration.

The activity of the cells is characterised by a slower uptake of the organic solids of the serum than of water, and a quicker uptake of the salts than of the water; but the absolute numerical relations vary in different regions of the intestine. The state of nutrition of the cells is the main factor in their activity; specific absorptive nerve-fibres were sought for, but not found. The absorption of water from the gut depends partly on the physical relation of the osmotic pressure of the solution in the intestine to that of the blood plasma; but even the absorption of water is influenced by the physiological regulation of this difference by the directing or, as it may be termed, orienting mechanism of the cells. Such orienting action was first noted in connection with salts by Otto Cohnheim; he showed that, in an intestinal loop with injured cells, sodium chloride enters its lumen from the blood though the same salt is being actively absorbed from a normal loop in the same animal at the same time. In all probability the cell activity which causes the organic constituents of serum to pass into the blood is of the same nature as that involved in the orienting action of the cells upon salts in solution.

Reid's conclusions with regard to the absorption of peptone and sugar are as follows:—The chief factor in the absorption of peptone is an assimilation (or absorption) by the cells, while in the absorption of glucose diffusion variable by the permeability of the cells (and so probably related to their physiological condition) is the main factor. By removal of the epithelium the normal ratio of peptone to glucose absorption is upset, and the value tends to approach that of diffusion of these substances through parchment paper into serum.

The fæces are alkaline, and contain the following substances :—

1. Water: in health from 68 to 82 per cent.; in diarrhœa it is more abundant still.

2. Undigested food; that is, if food is taken in excess, some escapes the action of the digestive juices. On a moderate diet unaltered proteid is never found.

3. Indigestible constituents of the food: cellulose, keratin, mucin, chlorophyll, gums, resins, cholesterin.

4. Constituents digestible with difficulty: uncooked starch, tendons, elastin, various phosphates, and other salts of the alkaline earths.

5. Products of decomposition of the food: indole, skatole, phenol, acids such as fatty acids, lactic acid, etc.; hæmatin from hæmoglobin; insoluble soaps like those of calcium and magnesium.

6. Bacteria of all sorts, and *débris* from the intestinal wall; cells, nuclei, mucus, etc.

7. Bile residues: mucus, cholesterin, traces of bile acids and their products of decomposition, stercobilin from the bile pigment.

The average quantity of solid fæcal matter passed by the human adult *per diem* is 6 to 8 ounces.

Meconium is the name given to the greenish-black contents of the intestine of new-born children. It is chiefly concentrated bile, with *débris* from the intestinal wall. The pigment is a mixture of bilirubin and biliverdin, not stercobilin.

CHAPTER XXXV

THE MECHANICAL PROCESSES OF DIGESTION

UNDER this head we shall study the neuro-muscular mechanism of the alimentary canal, which has for its object the onward movement of the food, and its thorough admixture with the digestive juices. We shall therefore have to consider mastication, deglutition, the movements of the stomach and intestines, defæcation, and vomiting.

MASTICATION.

The act of mastication is performed by the biting and grinding movement of the lower range of teeth against the upper. The simultaneous movements of the tongue and cheeks assist partly by crushing the softer portions of the food against the hard palate and gums, and thus supplement the action of the teeth, and partly by returning the morsels of food to the teeth again and again, as they are squeezed out from between them, until they have been sufficiently chewed.

The act of mastication is much assisted by the saliva, and the intimate incorporation of this secretion with the food is called *insalivation.*

Mastication is much more thoroughly performed by some animals than by others. Thus, dogs hardly chew their food at all, but the œsophagus is protected from abrasion by a thick coating of very viscid saliva which lubricates the pieces of rough food.

In vegetable feeders, on the other hand, insalivation is a much more important process. This is especially so in the ruminants; in these animals, the grass, etc., taken, is hurriedly swallowed, and passes into the first compartment of their four-chambered stomach. Later on, it is returned to the mouth in small instalments for thorough mastication and insalivation; this is the act of *rumination*, or "chewing the cud"; it is then once more swallowed and passes on to the digestive regions of the stomach.

In man, mastication is also an important process, and in people who have lost their teeth severe dyspepsia is often produced, which can be cured by a new set of teeth.

DEGLUTITION.

When properly masticated, the food is transmitted in successive portions to the stomach by the act of deglutition or swallowing. This, for the purpose of description, may be divided into *three* acts. In the first, particles of food collected as a bolus are made to glide between the surface of the tongue and the palatine arch, till they have passed the anterior arch of the fauces; in the second, the morsel is carried through the pharynx; and in the third, it reaches the stomach through the œsophagus. These three acts follow each other rapidly. (1.) The first act is voluntary, although it is usually performed unconsciously; the morsel of food when sufficiently masticated, is pressed between the tongue and palate, by the agency of the muscles of the former, in such a manner as to force it back to the entrance of the pharynx. (2.) The second act is the most complicated, because the food must go past the posterior orifice of the nose and the upper opening of the larynx without entering them. When it has been brought, by the first act, between the anterior arches of the palate, it is moved onwards by the movement of the tongue backwards, and by the muscles of the anterior arches contracting on it and then behind it. The root of the tongue being retracted, and the larynx being raised with the pharynx and carried forwards under the base of the tongue, the epiglottis is pressed over the upper opening of the larynx, and the morsel glides past it; the closure of the glottis is additionally secured by the simultaneous contraction of its own muscles: so that, even when the epiglottis is destroyed, there is little danger of food passing into the larynx so long as its muscles can act freely. In man, and some other animals, the epiglottis is not drawn as a lid over the larynx during swallowing. At the same time, the raising of the soft palate, so that its posterior edge touches the back part of the pharynx, and the approximation of the sides of the posterior palatine arch, which move quickly inwards like side curtains, close the passage into the upper part of the pharynx and the posterior nares, and form an inclined plane, along the under surface of which the morsel descends; then the pharynx, raised up to receive it, in its turn contracts, and forces it onwards into the œsophagus. The passage of the bolus of food through the three constrictors of the pharynx is the last step in this stage. (3.) In the third act, in which the food passes through the œsophagus, every part of that tube, as it receives the morsel and is dilated by it, is stimulated to contract: hence an undulatory or peristaltic contraction of the œsophagus occurs, which is easily observable through the skin in long-necked animals like the swan. If we suppose the bolus to be at one particular place in the tube, it acts stimulatingly on the circular muscular fibres behind it, and inhibitingly on those in front; the contraction therefore squeezes it into the dilated portion of the tube in front, where the same process is repeated, and this travels along the whole length of the tube. The second and third parts of the act of deglutition are involuntary. The action of these parts is more rapid than peristalsis usually is. This is due to the large amount of striated muscular tissue present. It serves the useful purpose of getting the bolus as quickly as possible past the opening of the respiratory tract.

Nervous Mechanism.—The nerves engaged in the reflex act of deglutition are:—*sensory*, branches of the fifth cranial nerve supplying the soft palate and tongue; glosso-pharyngeal, supplying the tongue and pharynx; the superior laryngeal branch of the vagus, supplying the epiglottis and the glottis; while the *motor* fibres concerned are:—branches of the fifth, supplying part of the digastric and mylo-hyoid muscles, and the muscles of mastication; the bulbar part of the spinal accessory through the pharyngeal plexus, supplying the levator palati, probably by rootlets which are glosso-pharyngeal in origin; the glosso-pharyngeal and vagus, and possibly the bulbar part of the spinal accessory, supplying the muscles of the pharynx through the pharyngeal plexus; the vagus, in virtue of its spinal accessory roots, supplying the muscles of the larynx through the inferior laryngeal branch; and the hypo-glossal, the muscles of the tongue. The nerve-centre by which the muscles are harmonised in their action, is situated in the medulla oblongata. Stimulation of the vagi gives rise to peristalsis of the œsophagus. The cell stations of these fibres are in the ganglion trunci vagi. Division of both pneumogastric nerves gives rise to paralysis of the œsophagus and stomach, and firm contraction of the cardiac orifice. These nerves therefore normally supply the œsophagus with motor, and the cardiac sphincter with inhibitory fibres. If food is swallowed after these nerves are divided, it accumulates in the gullet and never reaches the stomach.

In discussing peristalsis on a previous occasion (p. 158), we arrived at the conclusion that it is an inherent property of muscle rather than of nerve; though normally it is controlled and influenced by nervous agency. This nervous control is especially marked in the œsophagus; for if that tube is divided across, leaving the nerve branches intact, a wave of contraction will travel from one end to the other across the cut.

Swallowing of Fluids.—The swallowing both of solids and liquids is a muscular act, and can, therefore, take place in opposition to the force of gravity. Thus, horses and many other animals habitually drink up-hill, and the same feat can be performed by jugglers.

In swallowing liquids the two mylo-hyoid muscles form a diaphragm below the anterior part of the mouth. The stylo-glossi draw the tongue backwards and elevate its base; the two hyo-glossi act with these, pulling the tongue backwards and downwards. The action of these muscles resembles that of a force-pump projecting the mass of fluid down into the œsophagus; it reaches the cardiac orifice with great speed, and the pharyngeal and œsophageal muscles do not contract on it at all, but are inhibited during the passage of the fluid through them (Kronecker).

This is proved in a striking way in cases of poisoning by corrosive substances like oil of vitriol; the mouth and tongue are scarred and burnt, but the pharynx and œsophagus escape serious injury, so rapidly does the fluid pass along them; the cardiac orifice of the stomach is the next place to show the effects of the corrosive.

There is, however, no hard-and-fast line between the swallowing of solids and fluids: the more liquid the food is, the more does the force-pump action just described manifest itself.

Movements of the Stomach.

The gastric fluid is assisted in accomplishing its share in digestion by the movements of the stomach. In graminivorous birds, for example, the contraction of the strong muscular gizzard affords a necessary aid to digestion, by grinding and triturating the hard seeds which constitute their food. But in the stomachs of man and other Mammalia the movements of the muscular coat are too feeble to exercise any such mechanical force on the food; neither are they needed, for mastication has already done the mechanical work of a gizzard; and it has been demonstrated that substances are digested even when enclosed in perforated tubes, and consequently protected from mechanical influence.

When digestion is not going on, the stomach is uniformly contracted, its orifices not more firmly than the rest of its walls; but, if examined shortly after the introduction of food, it is found closely encircling its contents, and its orifices are firmly closed like sphincters. The cardiac orifice, every time food is swallowed, opens to admit its passage into the stomach, and immediately again closes. The pyloric orifice, during the first part of gastric digestion, is usually so completely closed, that even when the stomach is separated from the intestines, none of its contents escape. But towards the termination of the digestive process, the pylorus offers less resistance to the passage of substances from the stomach; first it yields to allow the successively digested portions to go through it; and then it allows the transit even of undigested substances. The peristaltic action of the muscular coat, whereby the digested portions are gradually moved towards the pylorus, also ensures thorough admixture with the gastric juice. The movements are observed to increase as the process of chymification advances, and are continued until it is completed.

The contraction of the fibres situated towards the pyloric end of the stomach is more energetic and more decidedly peristaltic than those of the cardiac portion. Thus, it was found in the case of St Martin, that when the bulb of a thermometer was placed about three inches from the pylorus, through the gastric fistula, it was tightly embraced from time to time, and drawn towards the pyloric orifice for a distance of three or four inches. The object of this movement appears to be, as just said, to carry the food towards the pylorus as fast as it is formed into chyme, and to propel the chyme into the duodenum; the undigested portions of food are kept back until they are also reduced into chyme, or until all that is digestible has passed out. The action of these fibres is often seen in the contracted state of the pyloric portion of the stomach after death, when it alone is contracted and firm, while the cardiac portion forms a dilated sac. Sometimes, by a predominant action of strong circular fibres placed between the cardia and pylorus, the two portions, or ends, as they are called, of the stomach, are partially separated from each other by a kind of hour-glass contraction.

The subject has recently been taken up by Cannon. He gave an animal food mixed with bismuth subnitrate, and obtained by the Röntgen rays shadow photographs of the stomach, because the bismuth salt renders its contents opaque. His results mainly confirm those of the earlier investigators; the principal peristalsis occurs in the pyloric portion of the stomach. The cardiac portion presses steadily on its contents, and as they become chymified, urges them onwards towards the pyloric portion; the latter empties itself gradually through the pylorus into the duodenum, and in the later stages of digestion the cardiac part also is constricted into a tube.

Under ordinary circumstances, three or four hours may be taken as the average time occupied by the digestion of a meal in the stomach. But the digestibility and quantity of the meal, and the state of body and mind of the individual, are important causes of variation. The pylorus usually opens for the first time about twenty minutes after digestion begins; it, however, quickly closes again. The acid chyme provides a chemical stimulus for pancreatic secretion, and the strongly alkaline pancreatic juice neutralises it; as soon as the intestinal contents are neutral, the pylorus again opens, more acid chyme is thrust into the duodenum; more pancreatic juice provided; and so on until the stomach is finally emptied.

Influence of the Nervous System.—The normal movements of the stomach during gastric digestion are in part controlled by the plexuses of nerves and ganglia contained in its walls. The stomach is also connected with the higher nerve-centres by means of branches of the vagi and of the splanchnic nerves through the solar plexus.

The vagi (especially the left) contain the acclerator nerves of the stomach; when they are stimulated the result is peristaltic movement. The sympathetic fibres are inhibitory; when they are stimulated peristalsis ceases. The cell stations on the course of the vagus fibres are in the ganglion trunci vagi; the post-ganglionic fibres that issue from this ganglion are non-medullated.

The sympathetic fibres leave the spinal cord by the anterior roots of the spinal nerves from the fifth to the eighth thoracic. They pass into the sympathetic system, have cell stations in the cœliac ganglion, and ultimately pass to the stomach by the splanchnic nerves.

It seems probable that automatic rhythmical contraction is inherent in the muscular coat of the stomach, and that the central nervous system is only employed to regulate it by impulses passing down by the vagi or splanchnic nerves.

The secretory nerves of the gastric glands are treated on p. 485.

VOMITING.

The expulsion of the contents of the stomach in vomiting, like that of mucus or other matter from the lungs in *coughing*, is preceded by an inspiration; the glottis is then closed, and immediately afterwards the abdominal muscles strongly act; but here occurs the difference in the two actions. Instead of the vocal cords yielding to the action of the abdominal muscles, they remain tightly closed. Thus the diaphragm, being unable to go up, forms an unyielding surface against which the stomach can be pressed. At the same time the *cardiac* sphincter being relaxed, and the orifice which it naturally guards being dilated, while the *pylorus* is closed, and the stomach itself also contracting, the action of the abdominal muscles expels the contents of the organ through the œsophagus, pharynx, and mouth. The reversed peristaltic action of the œsophagus possibly increases the effect.

It has been frequently stated that the stomach itself is quite passive during vomiting, and that the expulsion of its contents is effected solely by the pressure exerted upon it when the capacity of the abdomen is diminished by the contraction of the diaphragm, and subsequently of the abdominal muscles. The experiments and observations, however, which are supposed to confirm this statement, only show that the contraction of the abdominal muscles alone is sufficient to expel matters from an unresisting bag through the œsophagus; and that, under very abnormal circumstances, the stomach, by itself, cannot expel its contents. They by no means show that in ordinary vomiting the stomach is passive, for there are good reasons for believing the contrary. In some cases of violent vomiting the contents of the duodenum are passed by anti-peristalsis into the stomach, and are then vomited. Where there is obstruction to the intestine, as in strangulated hernia, the total contents of the small intestine may be vomited.

Nervous mechanism.—Some few persons possess the power of vomiting at will, or the power may be acquired by effort and practice. But normally the action is a reflex one.

The *afferent* nerves are principally the fifth, and glosso-pharyngeal (as in vomiting produced by tickling the fauces), and the vagus (as in vomiting produced by gastric irritants); but vomiting may occur from stimulation of other sensory nerves, *e.g.*, those from the kidney, uterus, testicle, etc. The centre may also be stimulated by impressions from the cerebrum and cerebellum, producing so-called *central* vomiting occurring in diseases of those parts.

The *centre* for vomiting is in the medulla oblongata, and coincides with the centres of the nerves concerned.

The *efferent* (motor) impulses are carried by the vagi to the stomach, by the phrenics to the diaphragm, and by various other spinal nerves to the abdominal muscles.

Emetics.—Some emetics produce vomiting by irritating the stomach; others, like tartar emetic, apomorphine, etc., by stimulating the vomiting centre.

Movements of the Intestines.

The movement of the intestines is *peristaltic* or *vermicular*, and is effected by the alternate contractions and dilatations of successive portions of the muscular coats. The contractions, which may commence at any point of the intestine, extend in a wave-like manner along the tube. They are similar to what we have described in the œsophagus. In any given portion, the longitudinal muscular fibres contract first, or more than the circular; they draw a portion of the intestine upwards, over the substance to be propelled, and then the circular fibres of the same portion contracting in succession from above downwards, press the substance into the portion next below, in which at once the same succession of actions next ensues. These movements take place slowly, and, in health, commonly give rise to no sensation; but they are perceptible when they are accelerated under the influence of any irritant.

The movements of the intestines are sometimes retrograde; and there is no hindrance to the backward movement of the contents of the small intestine, as in cases of violent vomiting just referred to.

But almost complete security is afforded against the passage of the contents of the large into the small intestine by the ileocæcal valve.

Proceeding from above downwards, the muscular fibres of the large intestine become, on the whole, stronger in direct proportion to the greater strength required for the onward moving of the fæces, which are gradually, owing to the absorption of water, becoming firmer. The greatest strength is in the rectum, at the termination of which the circular unstriped muscular fibres form a strong band called the *internal* sphincter; while an *external* sphincter muscle with striped fibres is placed rather lower down, and more externally, and holds the orifice closed by a constant slight tonic contraction.

Nervous mechanism.—Experimental irritation of the brain or cord produces no evident or constant effect on the movements of the intestines during life; yet in consequence of certain mental conditions the movements are accelerated or retarded; and in paraplegia the intestines appear after a time much weakened in their power, and costiveness, with a tympanitic condition, ensues.

As in the case of the œsophagus and stomach, the peristaltic movements of the intestines may be directly set up in the muscular fibres by the presence of food or chyme acting as the stimulus. Few or no movements occur when the intestines are empty.

The small intestines are connected with the central nervous system by the vagi and by the splanchnic nerves. The fibres which leave the medulla in the vagal rootlets are fine medullated ones: they arborise around cells in the ganglion trunci, whence non-medullated fibres continue the impulse to the intestinal walls; they pass through the solar plexus, but are not connected with nerve-cells in that plexus. In animals stimulation of the pneumogastric nerves induces peristaltic movements of the intestines. If the intestines are contracting peristaltically before the stimulus is applied, the movements are inhibited for a brief period, after which they are greatly augmented. The sympathetic fibres leave the cord as fine medullated fibres by the anterior roots from the sixth thoracic to the first lumbar, pass through the lateral chain, but do not reach their cell-stations until they arrive at the superior mesenteric ganglia: thence they pass as non-medullated fibres to the muscular coats. Stimulation of these fibres causes inhibition of any peristaltic movements that may be present. These nerves also contain vaso-motor fibres, and section of these leads to vaso-dilatation and a great increase of very watery succus entericus.

Peristalsis in the small intestine can be excited artificially even when all nerves running to it from the central nervous system have been cut through. After pinching any particular spot a wave of inhibition travels downwards, and a wave of contraction upwards. (Starling.)

In the case of the large intestine there is no supply from the vagus. The inferior mesenteric nerves are inhibitory in function, and the pelvic nerves take the place of the vagal fibres as excitatory: this refers to both coats of the muscular wall. If one pinches any particular spot, the upward wave of contraction is not so marked as in the small intestine, but the downward travelling wave of inhibition is well seen.

Duration of Intestinal Digestion.—The time occupied by the journey of a given portion of food from the stomach to the anus, varies considerably even in health, and on this account probably it is that such different opinions have been expressed in regard to the subject. About twelve hours are occupied by the journey of an ordinary meal through the *small* intestine, and twenty-four to thirty-six hours by the passage through the *large* bowel.

Drugs given for relief of diarrhœa or constipation act in various ways: some influence the amount of secretion and thus increase or diminish the fluidity of the intestinal contents; others acting on the muscular tissue or its nerves increase or diminish peristalsis.

The description just given of the intestinal movements relates to the principal movement observable, and which is of a peristaltic character. The rate of propagation of the peristaltic wave is slow but variable; it may be as small as 1 centimetre per minute.

Starling in his recent work on the subject has called attention to another kind of movement which he terms *swaying* or *pendulum* movement. These movements, and also the true peristaltic waves, may be seen in the small intestine in a warm saline bath even after all the nerves connecting them to the central nervous system have been cut through; the pendulum movements consist of slight waves of contraction affecting both muscular coats, and these are rapidly propagated at the rate of 2 to 5 centimetres per second. They cause a movement of the intestines from side to side, and occur at regular intervals of 5 or 6 seconds Their use appears to bring about a mixing of the intestinal contents; they are not able to move the contents onwards.

They differ from the true peristaltic waves in being *myogenic;* that is, they are due to the rhythmicality of the muscular fibres themselves, and are propagated from one muscular fibre to another. They are not abolished by painting the intestine with cocaine, or by an injection of nicotine. The true peristaltic waves cease under these circumstances, and they are, therefore, co-ordinated reflex actions, but as they continue after all nerves connecting the intestines to the central nervous system are severed, they must be carried out by the local nervous mechanism. This is the only example known of a true reflex action dependent on peripheral nervous structures.

Intestinal Oncometer.—To study the volume changes of vascular origin, a loop of intestine is enclosed in an oncometer like that described on p. 152 (fig. 179). This is a most valuable application of plethysmography, for the loop gives an accurate record of what is occurring in the splanchnic area.

Defæcation.—The act of the expulsion of fæces is in part due to an increased reflex peristaltic action of the lower part of the large intestine, namely, of the sigmoid flexure and rectum, and in part to the action of the abdominal muscles. In the case of active voluntary efforts, there is usually, first, an inspiration, as in the case of coughing, sneezing, and vomiting; the glottis is then closed, and the diaphragm fixed. The abdominal muscles are contracted, as in expiration; but as the glottis is closed, the whole of their pressure is exercised on the abdominal contents. The sphincter of the rectum being relaxed, the evacuation of its contents takes place accordingly, the effect being increased by the peristaltic action of the intestine.

Nervous Mechanism.—The anal sphincter muscle is normally in a state of tonic contraction. The nervous centre which governs this contraction is situated in the lumbar region of the spinal cord, inasmuch as in cases of division of the cord above this region the sphincter regains, after a time, to some extent the tonicity which is lost immediately after the operation. By an effort of the will, acting on the centre, the contraction may be relaxed or increased. Such voluntary control over the act is obviously impossible when the cord is divided. In ordinary cases the apparatus is set in action by the gradual accumulation of fæces in the sigmoid flexure and rectum, pressing by the peristaltic action of these parts of the large intestine against the sphincter, and causing by reflex action its relaxation; this sensory impulse acts upon the brain and reflexly through the spinal centre. At the same time that the sphincter is inhibited or relaxed, impulses pass to the muscles of the lower intestine increasing their peristalsis, and to the abdominal muscles as well.

Both inhibitory and motor fibres for the lower part of the intestine leave the cord by anterior roots lower than those which contain the fibres for the small intestine. The cell-stations are situated in the inferior mesenteric ganglia, or along the course of the colonic or hypogastric nerves. The lower portion of the large intestine resembles the œsophagus in being more under external nervous control than the small intestine.

CHAPTER XXXVI

THE URINARY APPARATUS

THIS consists of the kidneys; from each a tube called the *ureter* leads to the bladder in which the urine is temporarily stored; from the bladder a duct called the *urethra* leads to the exterior.

The Kidneys are two in number, and are situated deeply in the lumbar region of the abdomen on either side of the spinal column behind the peritoneum. They correspond in position to the last dorsal and three upper lumbar vertebræ; the right is slightly below the left in consequence of the position of the liver on the right side of the abdomen. They are about 4 inches long, 2½ inches broad, and 1½ inch thick. The weight of each kidney is about 4½ oz.

Structure.—The kidney is covered by a fibrous capsule, which is slightly attached at its inner surface to the proper substance of the organ by means of very fine bundles of areolar tissue and minute blood-vessels. From the healthy kidney, therefore, it may be easily torn off without much injury to the subjacent cortical portion of the organ. At the *hilus* of the kidney, it becomes continuous with the external coat of the upper and dilated part of the ureter (fig. 412).

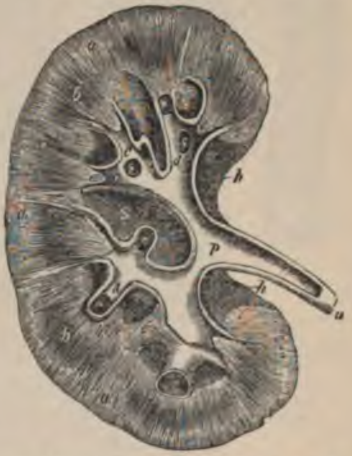

FIG. 412.—Plan of a longitudinal section through the pelvis and substance of the right kidney, ½: *a*, the cortical substance; *b*, *b*, broad part of the pyramids of Malpighi; *c*, *c*, the divisions of the pelvis named calyces, laid open; *c′*, one of those unopened; *d*, summit of the pyramid projecting into calyces; *e′*, *e*, section of the narrow part of two pyramids near the calyces; *p*, pelvis or enlarged portion of the ureter within the kidney; *u*, the ureter; *s*, the sinus; *h*, the hilus.

On dividing the kidney into two equal parts by a section carried through its long convex border it is seen to be composed of two portions called respectively *cortical* and *medullary;* the latter is composed of about a dozen conical bundles of urinary tubules, each bundle forming what is called a *pyramid.* The upper part of the *ureter* or duct of the organ is dilated into the *pelvis;* and this, again, after separating into two or three principal divisions, is finally subdivided into still smaller portions, varying in number from about 8 to 12, called *calyces.* Each of these little calyces or cups receives the pointed extremity or *papilla* of a pyramid. The number of pyramids varies in different animals; in some there is only one.

The kidney is a compound tubular gland, and both its cortical and medullary portions are composed of tubes, the *tubuli uriniferi,* which, by one extremity, in the *cortical* portion, commence around tufts of capillary blood-vessels, called *Malpighian bodies,* and, by the other, open through the papillæ into the pelvis of the kidney, and thus discharge the urine which flows through them. They are bound together by connective tissue.

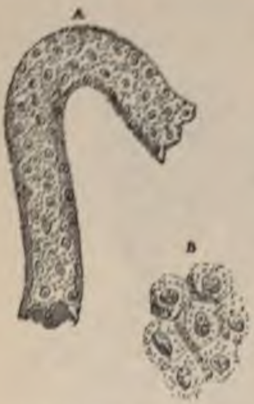

FIG. 418.—A. Portion of a secreting tubule from the cortical substance of the kidney. B. The epithelial or gland-cells. × 700 times.

In the pyramids the tubes are straight—uniting to form larger tubes as they descend through these from the cortical portion; while in the latter region they spread out more irregularly, and become much convoluted. But in the *boundary zone* between cortex and medulla, small collections of straight tubes called *medullary rays* project into the cortical region.

Tubuli Uriniferi.—The tubuli uriniferi (fig. 417) are composed of a basement membrane, lined internally by epithelium. They vary considerably in size in different parts of their course, but are, on an average, about $\frac{1}{600}$ of an inch ($\frac{1}{24}$ mm.) in diameter, and are found to be made up of several distinct portions which differ from one another very markedly, both in situation and structure.

Each begins in the cortex as a dilatation called the *Capsule of Bowman;* this encloses a tuft or glomerulus of capillaries called a *Malpighian corpuscle.* The tubule leaves the capsule by a *neck,* and then becomes convoluted (*first convoluted tubule*), but soon after becomes nearly straight or slightly spiral (*spiral tubule*); then rapidly narrowing it passes down into the medulla as the *descending tubule of Henle;* this turns round, forming a loop (*loop of Henle*), and passes up to the cortex again as the *ascending tubule of Henle.* It then becomes larger and irregularly zigzag (*zigzag tubule*) and again convoluted (*second convoluted tubule*). Eventually it narrows into a *junctional tubule*, which joins a straight or *collecting tubule.* This passes straight through the medulla, where it joins with others to form one of the *ducts of Bellini* that open at the apex of the pyramid. These parts are all shown in fig. 414.

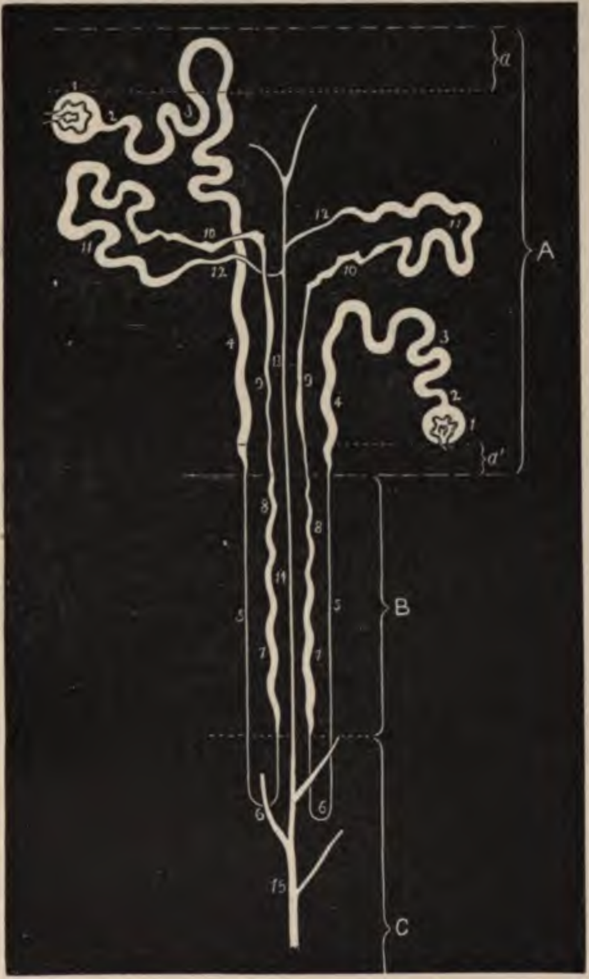

FIG. 414.—A diagram of the uriniferous tubes. A, cortex limited externally by the capsule; *a*, subcapsular layer not containing Malpighian corpuscles; *a'*, inner stratum of cortex, also without Malpighian capsules; B, boundary layer; C, medullary part next the boundary layer; 1, Bowman's capsule of Malpighian corpuscle; 2, neck of capsule; 3, first convoluted tubule; 4, spiral tubule; 5, descending limb of Henle's loop; 6, the loop proper; 7, thick part of the ascending limb; 8, spiral part of ascending limb; 9, narrow ascending limb in the medullary ray; 10, the zigzag tubule; 11, the second convoluted tubule; 12, the junctional tubule; 13, the collecting tubule of the medullary ray; 14, the collecting tube of the boundary layer; 15, duct of Bellini. (Klein.)

The character of the epithelium that lines these several parts of the tubules is as follows:—

In the *capsule*, the epithelium is flattened and reflected over the glomerulus.

The way in which this takes place in process of development is shown in figs. 415 and 416.

In the *neck* the epithelium is still flattened, but in some animals, like frogs, where the neck is longer, the epithelium is ciliated.

In the *first convoluted* and *spiral* tubules, it is thick, and the cells show a fibrillated structure, except around the nucleus, where the protoplasm is granular. The cells interlock laterally and are difficult to isolate. In some animals they are described as ciliated. In the *narrow descending tubule of Henle* and in *the loop* itself, the cells are clear and flattened and leave a considerable lumen; in the *ascending limb* they again become striated and nearly fill the tubule. In the *zigzag* and *second convoluted* tubules the fibrillations become even more marked. The *junctional* tubule has a large lumen, and is lined by clear flattened cells; the *collecting* tubules and *ducts of Bellini* are lined by clear cubical or columnar cells.

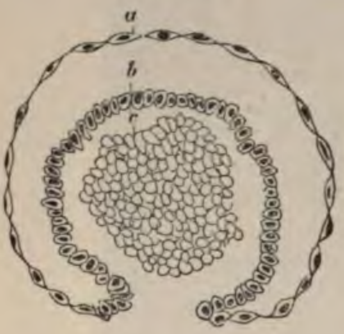

FIG. 415.—Transverse section of a developing Malpighian capsule and tuft (human). × 300. From a fœtus at about the fourth month; *a*, flattened cells growing to form the capsule; *b*, more rounded cells; continuous with the above, reflected round *c*, and finally enveloping it; *c*, mass of embryonic cells which will later become developed into blood-vessels. (W. Pye).

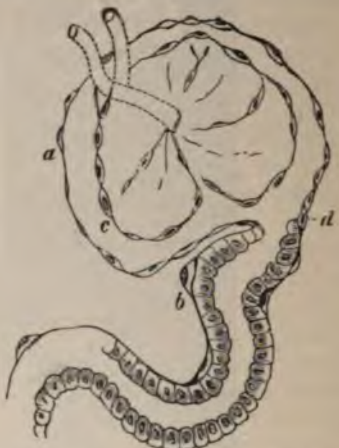

FIG. 416.—Epithelial elements of a Malpighian capsule and tuft, with the commencement of a urinary tubule showing the afferent and efferent vessel; *a*, layer of flat epithelium forming the capsule; *b*, similar, but rather larger epithelial cells, placed in the walls of the tube; *c*, cells, covering the vessels of the capillary tuft; *d*, commencement of the tubule, somewhat narrower than the rest of it. (W. Pye).

Blood-Vessels of Kidney.—The renal artery enters the kidney

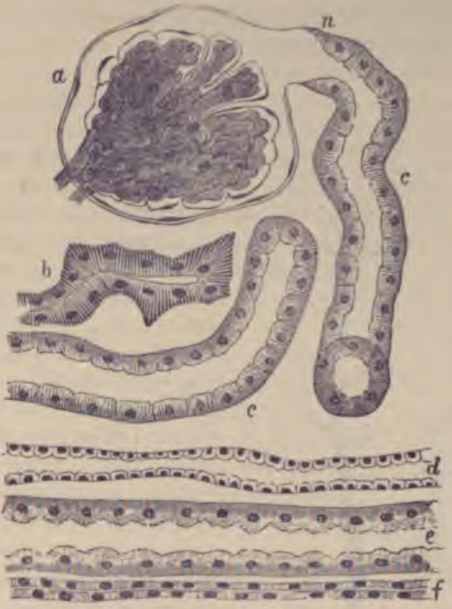

FIG. 417.—From a vertical section through the kidney of a dog—the capsule of which is supposed to be on the right. *a*, the capillaries of the Malpighian corpuscle, which are arranged in lobules; *n*, neck of capsule; *c*, convoluted tubes cut in various directions; *b*, zigzag tubule; *d*, *e*, and *f*, are straight tubes in a *medullary ray; d*, collecting tube; *e*, spiral tube; *f*, narrow section of ascending limb. × 380. (Klein and Noble Smith.)

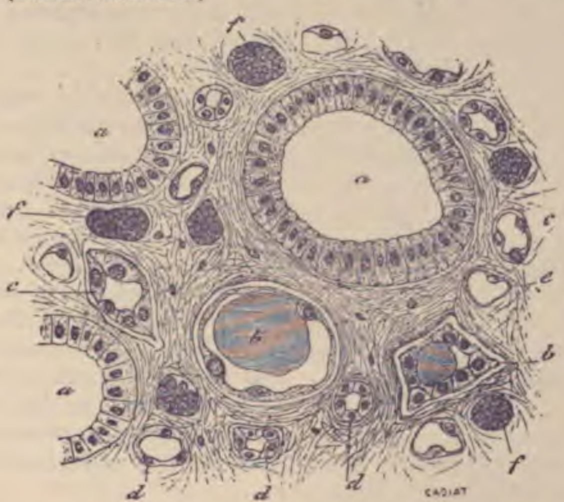

FIG. 418.—Transverse section of a renal papilla: *a*, large tubes or ducts of Bellini; *b*, *c*, and *d*, smaller tubes of Henle; *e*, *f*, blood capillaries, distinguished by their flatter epithelium. (Cadiat.)

at the hilus, and divides into branches that pass towards the cortex, then turn over and form incomplete arches in the region between cortex and medulla. From these arches vessels pass to the surface which are called the *interlobular arteries;* they give off vessels at right angles, which are the *afferent vessels of the glomeruli;* a glomerulus is made up of capillaries as previously stated. From each, a smaller vessel (*the efferent vessel of the glomerulus*) passes out, and like a portal vessel on a small scale, breaks up once more into capillaries which ramify between the convoluted tubules. These unite to form veins (*interlobular veins*) which accompany the interlobular arteries; they pass to venous arches, parallel to, but more complete than the corresponding arterial arches; they ultimately unite to form the renal vein that leaves the hilus. These veins receive also others which have a stellate arrangement near the capsule (*venæ stellulæ*).

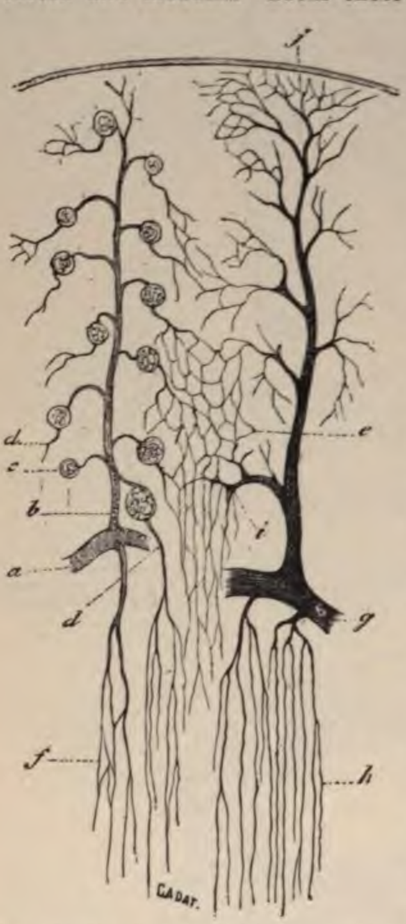

FIG. 419.—Vascular supply of kidney. *a*, part of arterial arch; *b*, interlobular artery; *c*, glomerulus; *d*, efferent vessel passing to the medulla as false arteria recta; *e*, capillaries of cortex; *f*, capillaries of medulla; *g*, venous arch; *h*, straight veins of medulla; *i*, interlobular vein; *j*, vena stellula. (Cadiat.)

The medulla is supplied by pencils of fine straight arterioles which arise from the arterial arches. They are called *arteriæ rectæ.* The efferent vessels of the glomeruli nearest the medulla may also break up into similar vessels which are called *false arteriæ rectæ.* The veins (*venæ rectæ*) take a similar course and empty themselves into the venous arches. In the boundary zone groups of *vasa recta* alternate with groups of tubules, and give a striated appearance to this portion of the medulla.

The Ureters.—The duct of each kidney, or *ureter,* is a tube about the size of a goose-quill, and from twelve to sixteen inches in length, which, continuous above with the pelvis, ends below by perforating obliquely the walls of the bladder, and opening on its internal surface.

It is constructed of three coats: (*a*) an outer *fibrous* coat; (*b*) a middle *muscular coat*, of which the fibres are unstriped, and arranged in three layers—the fibres of the central layer being circular, and those of the other two longitudinal in direction; the outermost longitudinal layer is, however, present only in the lower part of the ureter; and (*c*) a *mucous membrane* continuous with that of the pelvis above, and of the urinary bladder below. It is composed of areolar tissue lined by transitional epithelium.

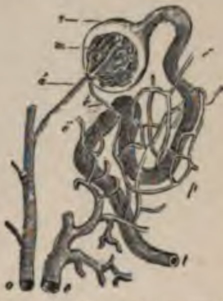

FIG. 420.—Diagram showing the relation of the Malpighian body to the uriniferous ducts and blood-vessels. *a*, one of the interlobular arteries; *a′*, afferent artery passing into the glomerulus; *c*, capsule of the Malpighian body, forming the commencement of and continuous with *t*, the uriniferous tube; *e′*, *e′*, efferent vessels which subdivide and form a plexus, *p*, surrounding the tube, and finally terminate in the branch of the renal vein *e*. (After Bowman.)

The Urinary Bladder, which forms a receptacle for the temporary lodgment of the urine, is pyriform; its widest part, which is situate above and behind, is termed the *fundus;* and the narrow constricted portion in front and below, by which it becomes continuous with the urethra, is called its *cervix* or *neck*.

It is constructed of four coats,—*serous*, *muscular*, *areolar* or *submucous*, and *mucous*. (*a*) The *serous* coat, which covers only the posterior and upper part of the bladder, has the same structure as the peritoneum, with which it is continuous. (*b*) The fibres of the *muscular* coat, which are unstriped, are arranged in three layers, of which the external and internal have a general longitudinal, and the middle layer a circular direction. The latter are especially developed around the *cervix* of the organ and form the *sphincter vesicæ*. (*c*) The *areolar* or *submucous* coat is constructed of connective-tissue with a large portion of elastic fibres. (*d*) The *mucous* membrane is like that of the ureters. It is provided with mucous glands, which are most numerous near the neck of the bladder.

The bladder is well provided with *blood- and lymph-vessels*, and with *nerves*. The latter consist of branches from the sacral and hypogastric plexuses. Ganglion cells are found, here and there, on the course of the nerve-fibres.

The Urethra.—This occupies the centre of the corpus spongiosum in the male. As it passes through the prostate it is lined by transitional, but elsewhere by columnar epithelium, except near the orifice, where it is stratified like the epidermis with which it becomes continuous. The female urethra has stratified epithelium throughout.

The epithelium rests on a vascular corium, and this is covered by submucous tissue containing an inner longitudinal and an outer circular muscular layer. Outside this a plexus of veins passes insensibly into the surrounding erectile tissue.

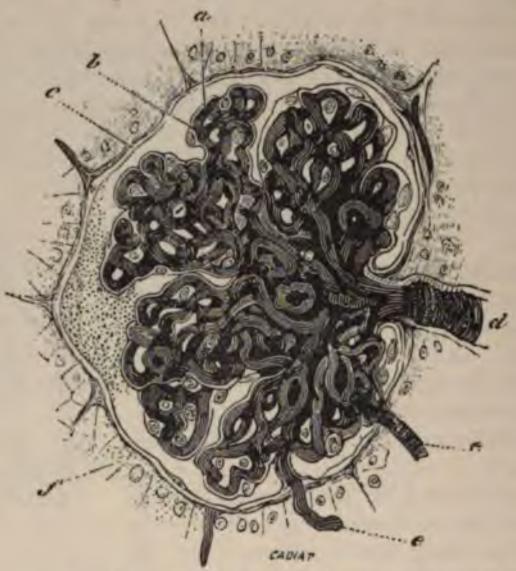

FIG. 421.—Malpighian corpuscle, injected through the renal artery with coloured gelatin; *a*, glomerular vessels; *b*, capsule; *c*, anterior capsule; *d*, afferent vessel of glomerulus; *e*, efferent vessels; *f*, epithelium of tubes. (Cadiat.)

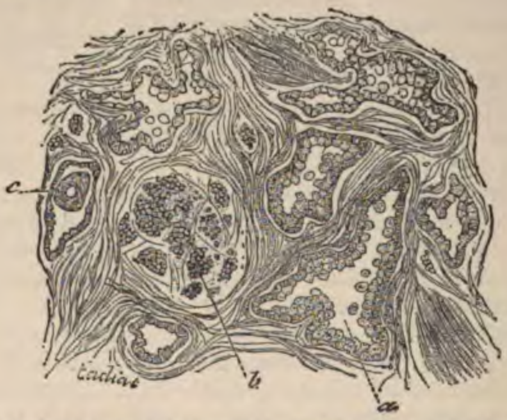

FIG. 422.—Section of a small portion of the prostate. *a*, gland duct cut across obliquely; *b*, gland structure; *c*, prostatic calculus. (Cadiat.)

Into the urethra open a number of oblique recesses or *lacunæ*, a number of small mucous glands (glands of Littré), two compound racemose glands (Cowper's glands), the glands of the prostate, and the vas deferens. *The prostate*, which surrounds the commencement of the male urethra, is a muscular and glandular mass. Its glands are tubular and lined by columnar epithelium.

THE FUNCTIONS OF THE KIDNEYS.

The main function of the kidneys is to separate the urine from the blood. The true secreting part of the kidney is the glandular epithelium that lines the convoluted portions of the tubules; there is in addition to this what is usually termed the filtering apparatus: we have already seen that the tufts of capillary blood-vessels called the Malpighian glomeruli are supplied with afferent vessels from the renal artery; the efferent vessels that leave these have a smaller calibre, and thus there is high pressure in the Malpighian capillaries. Certain constituents of the blood, especially water and salts, pass through the thin walls of these vessels into the surrounding Bowman's capsule which forms the commencement of each renal tubule. Though the process which occurs here is generally spoken of as a filtration, yet it is no purely mechanical process, but the cells exercise a selective influence, and prevent the albuminous constituents of the blood from escaping. During the passage of the water which leaves the blood at the glomerulus through the rest of the renal tubule, it gains the constituents urea, urates, etc., which are poured into it by the secreting cells of the convoluted tubules.

The term *excretion* is better than *secretion* as applied to the kidney, for the constituents of the urine are not actually formed in the kidney itself (as, for instance, the bile is formed in the liver), but they are formed elsewhere; the kidney is simply the place where they are picked out from the blood and eliminated from the body.

The Nerves of the Kidney.

Nerves.—The nerves of the kidney are derived from the renal plexus of each side. This consists of both medullated and non-medullated nerve-fibres, the former of varying size, and of nerve-cells. Fibres from the anterior roots of the eleventh, twelfth, and thirteenth dorsal nerves (in the dog) pass into this plexus. They are both vaso-constrictor and vaso-dilator in function. The nerve-cells on the course of the constrictor fibres are situated in the cœliac, mesenteric, and renal ganglia; the cells on the course of the dilator fibres are placed in the solar plexus and renal ganglia.

These nerves are thus vaso-motor in function; we have at present no knowledge of true secretory nerves to the kidney; the amount of urine varies directly with the blood-pressure in its capillaries.

Increase in the quantity of urine accompanies a rise of intra-capillary pressure. This may be produced by increasing the general blood-pressure; and this in turn may be produced in the following ways:—

(1.) By increase in the force or frequency of the heart-beat.

(2.) By constriction of the arterioles of areas other than that of the kidney, as in cold weather, when the cutaneous capillaries are constricted.*

(3.) By increase in the total contents of the vascular system, as after drinking large quantities of fluid.

The blood-pressure in the renal capillaries may also be increased locally by anything which leads to relaxation of the renal arterioles.

Decrease in the quantity of urine is produced by the opposites in each case.

If the renal nerves are divided, the renal arterioles are relaxed, and pressure in the renal capillaries is raised, so there is an increased flow of urine. This is accompanied by an increase in the volume of the kidney, as can be seen by the oncometer.

Stimulation of the divided nerves produces a diminution in the amount of urine, and a shrinkage of the kidney due to a constriction of its blood-vessels.†

If the splanchnic nerves are experimented with instead of the renal, the effects are not so marked, as these nerves have a wide distribution, and section leads to vascular dilatation in the whole splanchnic area; hence the increase in pressure in the renal capillaries is not so noticeable.

Puncture of the floor of the fourth ventricle in the neighbourhood of the vaso-motor centre (close to the spot, puncture of which produces glycosuria) leads to a relaxation of the renal arterioles and a consequent large increase of urine (polyuria).

Section of the spinal cord just below the medulla causes a cessation of secretion of urine, because of the great fall of general blood-pressure which occurs. If the animal is kept alive, however, blood-pressure goes up after a time, owing to the action of subsidiary vaso-motor centres in the cord. When this has occurred stimulation of the peripheral end of the cut spinal cord again causes urinary secretion to stop, because the renal artery (like the other arteries of the body) is so constricted that the pressure in the renal capillaries becomes too low for secretion to occur.

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* The reciprocal action between skin and kidneys will be discussed more fully in the chapter on the skin.

† The nerves also contain vaso-dilator fibres, which are excited when a slow rate of stimulation is used (see p. 307).

We thus see that the amount of urine varies with blood-pressure. But such a statement does not give the whole truth. Increase of blood-pressure and an increased amount of blood flowing through the kidney go together when the blood is circulating normally, and it is really the increase in the amount of blood which causes the rise in the amount of urine secreted. If the blood-pressure is increased without allowing the blood to flow, the amount of urine formed is not raised. This can be done by ligaturing the renal vein; the blood-pressure within the kidney then rises enormously, but the flow of urine stops.

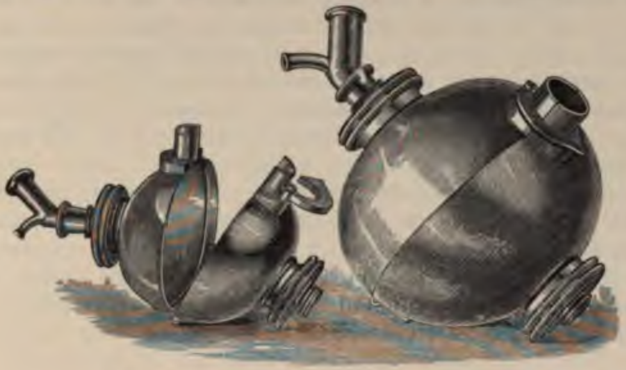

FIG. 423.—Oncometers for kidneys of different sizes.

The Oncometer is an instrument constructed on plethysmographic principles, by means of which the volume of the kidney is registered. The general characters of this instrument are described in the diagrams on p. 309. The special form adapted for the kidney is shown in fig. 423. An air oncometer connected with a Marey's tambour or a bellows recorder gives equally good or even better results.

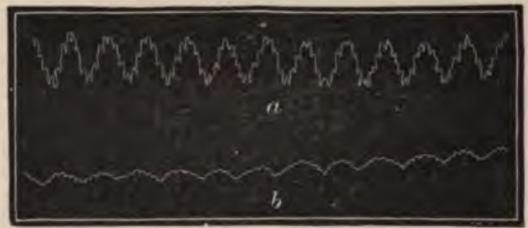

FIG. 424.—Curve taken by renal oncometer compared with that of ordinary blood-pressure. *a*, Kidney curve; *b*, blood-pressure curve. (Roy.)

It is found that the effect on the volume of the organ of dividing or stimulating nerves corresponds to blood-pressure. A rise of blood-pressure in the renal artery is produced by constriction of the renal arterioles; this is accompanied by a fall of pressure in the renal capillaries, and a shrinkage of the kidney. Increase in the volume of the kidney is produced by the opposite circumstances.

The accompanying tracing (fig. 424) shows that in a kidney curve one gets a rise of volume due to each heart-beat, and larger waves which accompany respiration. In many cases larger sweeping waves (Traube-Hering curves) are often shown as well. If a kidney curve is compared with a tracing of arterial pressure, it will be seen that the rise of arterial pressure coincides with a fall of the oncograph lever due to constriction of the renal vessels.

Diuretics are drugs which produce an increased flow of urine; they act in various ways, some by increasing the general blood-pressure, others by acting locally upon the kidney (increasing its volume as measured by the oncometer); under this latter head are doubtless to be included some also which act on the renal epithelium rather than on the blood-vessels.

Activity of the Renal Epithelium.

The epithelium of the convoluted tubules has a structure which suggests from its resemblance to other forms of secreting epitheliums, that its function here also is secreting. This is confirmed by the manner in which the blood-vessels break up into capillaries around these tubules; and is further confirmed by experiments.

Heidenhain showed that if a substance called sodium sulphindigotate, which ordinarily produces blue urine, is injected into the blood (after section of the medulla oblongata, which causes lowering of the blood-pressure in the renal glomeruli), when the kidney is examined, the cells of the convoluted tubules—and of these alone—are stained with the substance, which is also found in the lumen of the tubules. This shows that the pigment is eliminated by the cells of the convoluted tubules, and that when by diminishing the blood-pressure, the filtration of urine is stopped, the pigment remains in the convoluted tubes, and is not, as it would be under ordinary circumstances, swept away from them by the flushing of them by the watery part of the urine derived from the glomeruli. It therefore is probable that the cells, if they excrete the pigment, excrete urea and other substances also.

But the proof is not absolute, for the pigment is a foreign substance. Urea is a very difficult substance to trace in this way because it does not leave any coloured trail behind it. In birds the place of urea is taken by uric acid, and the urates can be actually traced, because they are deposited as crystals, and can be seen in the cells and convoluted tubes much in the same way as Heidenhain's blue pigment.

Other experiments, however, have been undertaken to prove the point for the case of urea.

If the part of the cortex of the kidney which contains the glomeruli is removed, urea still continues to be formed. This is a proof that the excretion is performed by the portions of the convoluted tubules that remain.

By using the kidney of the frog or newt, which has two distinct vascular supplies, one from the renal artery to the glomeruli, and the other from the renal-portal vein to the convoluted tubes, Nussbaum stated that certain foreign substances, *e.g.* peptones and sugar, when injected into the blood, are eliminated by the glomeruli, and so are not got rid of when the renal arteries are tied; whereas certain other substances, *e.g.* urea, when injected into the blood, are eliminated by the convoluted tubes, even when the renal arteries have been tied. These experiments have, however, been subjected to considerable criticism, and some observers have failed to obtain the same result. A re-investigation of the subject has been recently undertaken by Dr A. P. Beddard. He finds that ligature of all the arteries to the kidneys in the frog cuts the glomeruli completely out of the circulation. Adami's failure to confirm Nussbaum was due, not as he supposed to anastomoses between the terminations of the renal artery and the renal-portal system, but to incomplete ligature of the arteries. When the glomeruli are shut off in this way, no secretion takes place either spontaneously or after injection of urea, which is a diuretic; the contrary results obtained by Nussbaum were due to imperfect ligature, so that a number of glomeruli were left intact. Nussbaum's anatomical facts were therefore right, but his physiological experiments were faulty. A certain supply of arterial blood is necessary to the normal life of the renal epithelium, for this undergoes fatty degeneration and comes away (desquamates) in consequence of the occlusion of the glomeruli. Beddard's experiments, though important, do not really settle the question concerning the normal function of the epithelium of the tubules; they suggest that another series of experiments must be undertaken, in which an adequate supply of oxygen to the epithelium is ensured after complete ligature of all the arteries.

The Work done by the Kidney.

We have already seen (p. 321) the great importance a study of osmosis in the body has in the understanding of many physiological facts.

The urine is separated from the blood by a process which is not simply filtration, and if we measure the work of the kidney it is found to be vastly greater than could be produced by the intra-capillary blood-pressure. Ludwig held that re-absorption of some of the water and salts which escape at the glomeruli takes place in the tubules. Cushny finds this may occur to some extent, but the main function of the tubules is undoubtedly secretion, not absorption.

The work done by the kidney cells in order to separate from the blood-plasma a fluid with the much higher osmotic pressure of urine can be estimated.

We may take some examples from Dreser's work. He took the case in which 200 c.c. of urine were excreted during a night; the blood plasma in this case had an osmotic pressure = 0·92 per cent. solution; while that of the urine was = 4·0 per cent. solution of sodium chloride. To measure the work of the kidney we may take the mean of 0·92 and 4 as the average concentration of the salt during the process of excretion, and thus it is found that the kidney did about 18 kilogramme-metres of work. In another case of more concentrated urine obtained from a cat previously deprived of water for three days, the numbers were respectively 1·1 and 8·0. The difference was equal to a pressure of 498 metres of water; so that at the end the kidney had separated urine from the blood against a pressure of 49,800 grammes per square centimetre, a force about six times greater than the maximum force of muscle.

Extirpation of the Kidneys.

Extirpation of one kidney for stone, etc., is a common operation. It is not followed by any untoward result. The remaining kidney enlarges and does the work previously shared between the two.

Extirpation of both kidneys is fatal; the urea, etc., accumulate in the blood, and the animal dies in a few days; uræmic convulsions (see p. 556) do not occur in such experiments.

Ligature of both renal arteries amounts to the same thing as extirpation of the kidneys, and leads to the same result. If the ligature is released the kidney once more sets to work, but the urine secreted at first is albuminous, owing to the epithelium having been impaired by being deprived for a time of its blood supply.

Removal of one kidney, followed at a later period by removal of a half or two-thirds of the other, leads in dogs, in which the operation has been performed by Bradford, to a surprising result. After the second operation the urine is increased in amount, and the quantity of urea is much greater than normal. This comes from a disintegration of the nitrogenous tissues; the animal wastes rapidly and dies in a few weeks. It is thus evident that the kidneys play an important rôle in nitrogenous metabolism apart from merely excreting waste substances. The exact explanation has still to be found, but it is possible that the kidney, like the pancreas and liver, and many ductless glands, forms an internal secretion (see p. 328).

The Passage of Urine into the Bladder.

As each portion of urine is secreted it propels that which is already in the uriniferous tubes onwards into the pelvis of the kidney. Thence through the ureter the urine passes into the bladder, into which its rate and mode of entrance has been watched in cases of *ectopia vesicæ, i.e.* of such fissures in the anterior and lower part of the walls of the abdomen, and of the front wall of the bladder, as expose to view its hinder wall together with the orifices of the ureters. The urine does not enter the bladder at any regular rate, nor is there a synchronism in its movement through the two ureters. During fasting, two or three drops enter the bladder every minute; each drop as it enters first raises up the little papilla through which the ureter opens, and then passes slowly through its orifice, which at once again closes like a sphincter. In the recumbent posture, the urine collects for a little time in the ureters, then flows gently, and, if the body is raised, runs from them in a stream till they are empty. Its flow is aided by the peristaltic contractions of the ureters, and is increased in deep inspiration, or by straining, and in active exercise, and in fifteen or twenty minutes after a meal. The urine is prevented from regurgitation into the ureters by the mode in which these pass through the walls of the bladder, namely, by their lying for between half and three-quarters of an inch between the muscular and mucous coats before they turn rather abruptly forwards, and open through the latter into the interior of the bladder.

Micturition.

The contraction of the muscular walls of the bladder may by itself expel the urine with little or no help from other muscles. In so far, however, as it is a *voluntary* act, it is performed by means of the abdominal and other expiratory muscles, which in their contraction press on the abdominal viscera, the diaphragm being fixed, and cause the expulsion of the contents of those whose sphincter muscles are at the same time relaxed. The muscular coat of the bladder co-operates, in micturition, by reflex *involuntary* action, with the abdominal muscles; and the act is completed by the *accelerator urinæ*, which, as its name implies, quickens the stream, and expels the last drop of urine from the urethra. The act, so far as it is not directed by volition, is under the control of a nervous *centre* in the lumbar spinal cord, through which, as in the case of the similar centre for defæcation, the various muscles concerned are harmonised in their action. It is well known that the act may be reflexly induced, *e.g.* in children who suffer from intestinal worms, or other such irritation. Generally the afferent impulse which calls into action the desire to micturate is excited by over-distension of the bladder, or even by a few drops of urine passing into the urethra. The impulse passes up to the lumbar centre, and produces, on the one hand, inhibition of the sphincter, and on the other hand contraction of the necessary muscles for the expulsion of the contents of the bladder. The tonic action of the lumbar centre can also be inhibited by the will.

The bladder receives nerves from two sources:—(1) from the lower dorsal and upper lumbar nerves; these fibres pass to the sympathetic chain, from here to the inferior mesenteric ganglion, and ultimately reach the bladder by the hypogastric nerves. Stimulation of these nerves causes contraction of the circular fibres of the bladder, including the sphincter; (2) from the second and third sacral nerves; these run to the bladder by the nervi erigentes. Stimulation of these nerves causes relaxation of the sphincter and contraction of the detrusor urinæ. (Zeissl.) Langley and Anderson find, however, that stimulation of both sets of nerves causes contraction of both longitudinally and circularly arranged muscle bundles.

CHAPTER XXXVII

THE URINE

Quantity.—A man of average weight and height passes from 1400 to 1600 c.c., or about 50 oz. daily. This contains about 50 grammes (1½ oz.) of solids. For analytical purposes it should be collected in a tall glass vessel capable of holding 3000 c.c., which should have a smooth-edged neck accurately covered by a ground-glass plate to exclude dust and prevent evaporation. The vessel, moreover, should be graduated so that the amount may be easily read off. From the total quantity thus collected in the twenty-four hours, samples should be drawn off for examination.

Colour.—This is some shade of yellow which varies considerably in health with the concentration of the urine. It is due to a mixture of pigments; of these urobilin is the one of which we have the most accurate knowledge. Urobilin has a reddish tint, and is undoubtedly derived from the blood pigment, and, like bile pigment, is an iron-free derivative of hæmoglobin. The theory usually accepted concerning its mode of origin is that bile pigment is in the intestines converted into stercobilin; that most of the stercobilin leaves the body with the fæces; that some is reabsorbed and is excreted with the urine as urobilin. Both stercobilin and urobilin are very like the artificial reduction product of bilirubin called hydrobilirubin (see p. 511). Normal urine, however, contains very little urobilin. The actual body present is a chromogen or mother substance called urobilinogen, which by oxidation—for instance, standing exposed to the air—is converted into the pigment proper. In certain diseased conditions the amount of urobilin is considerably increased.

The most abundant urinary pigment is a yellow one, named *urochrome*. It shows no absorption bands. It is probably an oxidation product of urobilin. (Riva, A. E. Garrod.)

Reaction.—The reaction of normal urine is acid. This is not due to free acid, as the uric and hippuric acids in the urine are combined as urates and hippurates respectively. The acidity is due to acid salts, of which acid sodium phosphate is the most important. Under certain circumstances the urine becomes less acid and even alkaline; the most important of these are as follows:—

1. During digestion. Here there is a formation of free acid in the stomach, and a corresponding liberation of bases in the blood, which, passing into the urine, diminish its acidity, or even render it alkaline. This is called *the alkaline tide;* the opposite condition, *the acid tide*, occurs after a fast—for instance, before breakfast.

2. In herbivorous animals and vegetarians. The food here contains excess of alkaline salts of acids like tartaric, citric, malic, etc. These acids are oxidised into carbonates, which, passing into the urine, give it an alkaline reaction.

Specific Gravity.—This should be taken in a sample of the twenty-four hours' urine with a urinometer.

The specific gravity varies inversely as the quantity of urine passed under normal conditions from 1015 to 1025. A specific gravity below 1010 should excite suspicion of hydruria; one over 1030, of a febrile condition, or of diabetes, a disease in which it may rise to 1050. The specific gravity has, however, been known to sink as low as 1002 (after large potations, *urina potus*), or to rise as high as 1035 (after great sweating) in perfectly healthy persons.

Composition.—The following table gives the average amounts of the urinary constituents passed by a man in the twenty-four hours:—

Total quantity of urine	1500·00	grammes.
Water	1440·00	,,
Solids	60·00	,,
Urea	35·00	,,
Uric acid	0·75	,,
Sodium chloride	16·5	,,
Phosphoric acid	3·5	,,
Sulphuric acid	2·0	,,
Ammonia	0·65	,,
Creatinine	0·9	,,
Chlorine	11·0	,,
Potassium	2·5	,,
Sodium	5·5	,,
Calcium	0·26	,,
Magnesium	0·21	,,

The most abundant constituents of the urine are water, urea, and sodium chloride. In the foregoing table one must not be misled by seeing the names of the acids and metals separated. The acids and the bases are combined to form salts, such as urates, chlorides, sulphates, phosphates, etc.

Urea.

Urea, or **Carbamide,** $CO(NH_2)_2$, is isomeric (that is, has the same empirical, but not the same structural formula) with ammonium cyanate (NH_4) CNO, from which it was first prepared synthetically by Wöhler in 1828. Since then it has been prepared synthetically in other ways. Wöhler's observation derives interest from the fact that this was the first organic substance which was prepared synthetically by chemists.*

When crystallised out from the urine it is found to be readily soluble both in water and alcohol: it has a saltish taste, and is neutral to litmus paper. The form of its crystals is shown in fig. 425.

When treated with nitric acid, nitrate of urea ($CON_2H_4.HNO_3$) is formed; this crystallises in octahedra, lozenge-shaped tablets or hexagons (fig. 426). When treated with oxalic acid, flat or prismatic crystals of urea oxalate ($CON_2H_4.H_2C_2O_4 + H_2O$) are formed (fig. 427).

These crystals may be readily obtained by adding excess of the respective acids to urine which has been concentrated to a third or a quarter of its bulk.

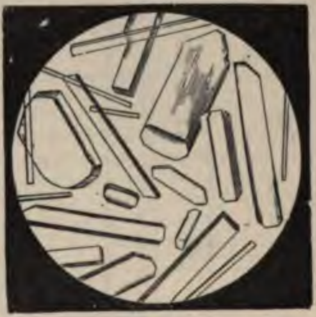

FIG. 425.—Crystals of Urea.

Under the influence of an organised ferment, the torula or micrococcus ureæ, which grows readily in stale urine, urea takes up water, and is converted into ammonium carbonate [$CON_2H_4 + 2H_2O = (NH_4)_2CO_3$]. Hence the ammoniacal odour of putrid urine.

By means of nitrous acid, urea is broken up into carbonic acid, water and nitrogen, $CON_2H_4 + 2HNO_2 = CO_2 + 3H_2O + 2N_2$. The evolution of gas bubbles which takes place on the addition of fuming nitric acid may be used as a test for urea.

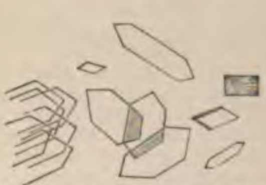

FIG. 426.—Crystals of Urea nitrate.

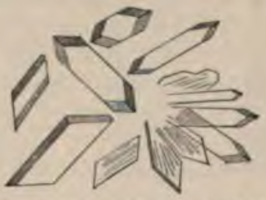

FIG. 427.—Crystals of Urea oxalate.

Hypobromite of soda decomposes urea in the following way:—

$$\underset{\text{[Urea.]}}{CON_2H_4} + \underset{\text{[Sodium hypobromite.]}}{3NaBrO} = \underset{\text{[Carbonic acid.]}}{CO_2} + \underset{\text{[Nitrogen.]}}{N_2} + \underset{\text{[Water.]}}{2H_2O} + \underset{\text{[Sodium bromide.]}}{3NaBr.}$$

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[*] Meldola has pointed out that the English chemist Henry Hennell prepared alcohol from olefiant gas simultaneously with Wöhler's synthesis of urea. The honour of founding the science of organic chemistry must, therefore, be shared between the two men.

This reaction is important, for on it one of the readiest methods for estimating urea depends. There have been various pieces of apparatus invented for rendering the analysis easy; but the one described below is the best. If the experiment is performed as directed, nitrogen is the only gas that comes off, the carbonic acid being absorbed by excess of soda. The amount of nitrogen is a measure of the amount of urea.

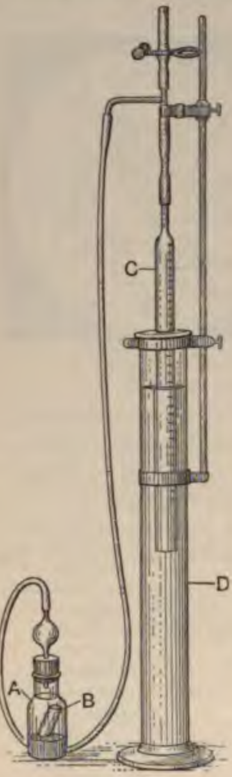


FIG. 428.—Dupré's Urea Apparatus.

Dupré's apparatus (fig. 428) consists of a bottle (A) united to a measuring tube by indiarubber tubing. The measuring tube (C) is placed within a cylinder of water (D), and can be raised and lowered at will. Measure 25 c.c. of alkaline solution of sodium hypobromite (made by mixing 2 c.c. of bromine with 23 c.c. of a 40 per cent. solution of caustic soda) into the bottle A. Measure 5 c.c. of urine into a small tube (B), and lower it carefully, so that no urine spills, into the bottle. Close the bottle securely with a stopper perforated by a glass tube; this glass tube (the bulb blown on this tube prevents froth from passing into the rest of the apparatus) is connected to the measuring tube by indiarubber tubing and a T-piece. The third limb of the T-piece is closed by a piece of indiarubber tubing and a pinch-cock, seen at the top of the figure. Open the pinch-cock and lower the measuring tube until the surface of the water with which the outer cylinder is filled is at the zero point of the graduation. Close the pinch-cock, and raise the measuring tube to ascertain if the apparatus is air-tight. Then lower it again. Tilt the bottle A so as to upset the urine, and shake well for a minute or so. During this time there is an evolution of gas. Then immerse the bottle in a large beaker containing water of the same temperature as that in the cylinder. After two or three minutes raise the measuring tube until the surfaces of the water inside and outside it are at the same level. Read off the amount of gas (nitrogen) evolved. 35·4 c.c. of nitrogen are yielded by 0·1 gramme of urea. From this the quantity of urea in the 5 c.c. of urine and the percentage of urea can be calculated. If the total urea passed in the twenty-four hours is to be ascertained, the twenty-four hours' urine must be carefully measured and thoroughly mixed. A sample is then taken from the total for analysis; and then, by a simple sum in proportion, the total amount of urea is ascertained.

Another method (Liebig's) of estimating urea in urine is the following:—Take 40 c.c. of urine; add to this 20 c.c. of baryta mixture (two volumes of barium hydrate and one of barium nitrate, both saturated in the cold). Filter off the precipitate of barium phosphate and sulphate which is formed. Take 15 c.c. of the filtrate (this corresponds to 10 c.c. of urine) in a beaker. Run into it from a burette standard mercuric nitrate solution of such a strength that 1 c.c. exactly precipitates 0·01 gramme of urea as a compound with the formula $(CON_2H_4)_2Hg(NO_3)_2(HgO)_3$. The solution is run in until the precipitate ceases to form, and free mercuric nitrate is present in the mixture; this can be detected by the yellow colour a drop of the mixture gives with a drop of saturated solution of sodium carbonate on a white slab. The amount used from the burette can be read off, and the percentage of urea calculated. In another specimen of the same urine, the chlorides are then estimated, and 1 gramme of urea subtracted for every 1·3 gramme of sodium chloride formed.

These two methods give nearly identical results; the former is the easier to perform, and the results are sufficiently accurate for ordinary purposes.

A more accurate determination can be best made by the method introduced by Mörner and Sjöquist. The following reagents, etc., are wanted :—(i.) A saturated solution of barium chloride containing 5 per cent. of barium hydrate ; (ii.) A mixture of alcohol and ether in the proportion 2 : 1 ; (iii.) The apparatus, etc., necessary for carrying out Kjeldahl's method of estimating nitrogen. 5 c.c. of urine are mixed with 5 c.c. of the barium mixture, and 100 c.c. of the ether-alcohol mixture. By this means all nitrogenous substances except urea are precipitated. Twenty-four hours later this is filtered off, and the precipitate is washed with 50 c.c. of the ether-alcohol mixture. The washings are added to the filtrate, and a little magnesia is added to drive off ammonia. The fluid is then evaporated down at 55° C. until its volume is about 10 c.c., and the nitrogen in this estimated by Kjeldahl's method. The nitrogen found is multiplied by 2·143, and the result is the amount of the urea.

Kjeldahl's method of estimating nitrogen consists in boiling the material under investigation with strong sulphuric acid. The nitrogen present is by this means converted into ammonia. Excess of soda is then added, and the ammonia distilled over into a known volume of standard acid. The amount of diminution of acidity in the standard enables one to calculate the amount of ammonia, and thence the amount of nitrogen.

The quantity of urea is variable, the chief cause of variation being the amount of proteid food ingested. In a man in a state of nitrogenous equilibrium, taking daily 100 grammes of proteid in his food, the quantity of urea secreted daily is about 33 to 35 grammes (500 grains). The normal percentage in human urine is 2 per cent.; but this also varies, because the concentration of the urine varies considerably in health. In dogs it may be 10 per cent. The excretion of urea is usually at a maximum three hours after a meal, especially after a meal rich in proteids. The urea does not come, however, direct from the food; the food must be first assimilated, and become part of the body, before it can break down to form urea. Food increases the elimination of urea because it stimulates the tissues to increased activity; their waste nitrogenous products are converted into urea, which, passing into the blood, is directly excreted by the kidneys. The greater the amount of proteid food given, the more waste products do the tissues discharge from their protoplasm, in order to make room for the new proteid which is built into its substance. Recent experiments by Chittenden and others have shown that nitrogenous equilibrium can be maintained on a diet containing only half the usual amount of proteid. In such people the excretion of urea falls correspondingly, the other nitrogenous constitutents of the urine remaining fairly constant.

Muscular exercise has little immediate effect on the amount of urea discharged. In very intense muscular work there is a slight immediate increase of urea, but this is quite insignificant when compared to the increase of work. This is strikingly different from what occurs in the case of carbonic acid; the more the muscles work, the more carbonic acid do they send into the venous blood, which is [illegible] careful research has [illegible] genuine [illegible] does occur in [illegible] only a slight [illegible] are excreted during the [illegible]

Where is Urea formed? [illegible] considered that it [illegible] formerly thought that [illegible] and Dumas were [illegible] of the kidneys the [illegible] in the blood and [illegible] the kidneys cease [illegible] is taken [illegible] the patient [illegible]

[illegible] no [illegible] impression of [illegible]

[illegible] fairly large [illegible] discharged [illegible] normal urine; [illegible] the creatine in [illegible] as urea: moreover, [illegible] the laboratory.

Similarly, other [illegible] organs, [illegible], lymphatic glands, secreting glands, participate in the formation of urea; but the most important appears to be the liver: this is the organ where the final changes take place. The urea is then carried by the blood to the [illegible], and is there excreted.

[illegible] facts of experiment and of pathology point very strongly in support of the theory that urea is formed in the liver. The principal are the following:—

1. After removal of the liver in such animals as frogs, urea formation almost ceases, and ammonia is found in the urine instead.

2. In mammals, the extirpation of the liver is such a severe operation that the animals do not live. But the liver of mammals can be very largely thrown out of gear by connecting the portal vein directly to the inferior vena cava (Eck's fistula). This experiment has been done successfully in dogs; the amount of urea in the urine is lessened, and its place is taken by ammonia.

3. When degenerative changes occur in the liver, as in *cirrhosis* of that organ, the urea formed is much lessened, and its place is taken by ammonia. In *acute yellow atrophy* urea is almost absent in the urine, and, again, there is considerable increase in the ammonia. In this disease leucine and tyrosine are also found in the urine; undue stress should not be laid upon this latter fact, for the leucine and tyrosine doubtless originate in the intestine, and, escaping further decomposition in the degenerated liver, pass as such into the urine.

We have to consider next the intermediate stages between proteid and urea. A few years ago Drechsel succeeded in artificially producing urea from casein. More recent work has shown that this is true for other proteids also. If a proteid is decomposed by hydrochloric acid, a little stannous chloride being added to prevent oxidation, a number of products are obtained, such as ammonium salts, leucine, tyrosine, aspartic, and glutaminic acids. This was known before, so the chief interest centres round two new substances, precipitable by phosphotungstic acid. One of these is called *lysine* ($C_6H_{14}N_2O_2$, di-amino-caproic acid); the other was first called *lysatinine*. Hedin then showed that lysatinine is a mixture of lysine with another base called *arginine* ($C_6H_{14}N_4O_2$); it is from the arginine that the urea comes in the experiment to be next described. Arguing from some resemblances between this substance and creatine, Drechsel expected to be able to obtain urea from it, and his expectation was confirmed by experiment. He took a silver compound of the base, boiled it with barium carbonate, and after twenty-five minutes' boiling obtained urea. (See note on p. 573.)

It is, however, extremely doubtful whether the chemical decompositions produced in laboratory experiments on proteids are comparable to those occurring in the body. Many physiologists consider that the amino-acids are intermediate stages in the metabolic processes that lead to the formation of urea from proteids. We have already alluded to this question in relation to the creatine of muscle, and we are confronted with the difficulty that injection of creatine into the blood leads to an increase not of urea, but of creatinine in the urine. If creatine is an intermediate step, it must undergo some further change before it leaves the muscle. Other amino-acids, such as glycine (amino-acetic acid), leucine (amino-caproic acid), and arginine are probably to be included in the same category; there is, however, no evidence that tyrosine acts in this way. The facts upon which such a theory depends are (1) that the introduction of glycine or leucine into the bowel, or into the circulation, leads to an increase of urea in the urine; and (2) that amino-acids appear in the urine of patients suffering from acute yellow atrophy of the liver. Then, again, it is perfectly true that, in the laboratory, urea can be obtained from creatine, and also from uric acid, but such experiments do not prove that creatine or uric acid are normally intermediate products of urea formation in the body. Still, if we admit, for the sake of argument, that amino-acids are normally intermediate stages in proteid metabolism, and glance at their formulæ—

Glycine	$C_2H_5NO_2$,
Leucine	$C_6H_{13}NO_2$,
Creatine	$C_4H_9N_3O_2$,

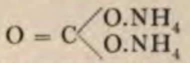
—we see that the carbon atoms are more numerous than the nitrogen atoms. In urea, CON_2H_4, the reverse is the case. The amino-acids must therefore be split into simpler compounds, which unite with one another to form urea. Urea formation is thus, in part, synthetic. There have been various theories advanced as to what these simpler compounds are. Some have considered that cyanate, others that carbamate, and others still that carbonate of ammonium is formed. Schröder's work, which has been confirmed by subsequent investigators, proves that ammonium carbonate is one of the urea precursors, if not the principal one. The equation which represents the reaction is as follows:—

$$\underset{\text{[Ammonium carbonate.]}}{(NH_4)_2CO_3} - \underset{\text{[Water.]}}{2H_2O} = \underset{\text{[Urea.]}}{CON_2H_4}.$$

Schröder's principal experiment was this: a mixture of blood and ammonium carbonate was injected into the liver by the portal vein; the blood leaving the liver by the hepatic vein was found to contain urea in great abundance. This does not occur when the same experiment is performed with any other organ of the body, so that Schröder's experiments also prove the great importance of the liver in urea formation.

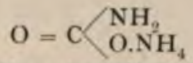
There is, however, no necessity to suppose that the formation of amino-acids is a necessary preliminary to urea formation. The conversion of the leucine and arginine formed in the intestine into ammonium salts and then into urea does certainly occur, but this only accounts for quite an insignificant fraction of the urea in the urine. If the same occurs in tissue metabolism, we ought to find considerable quantities of leucine, glycine, creatine, arginine, and such substances in the blood, leaving the various tissues and entering the liver; but we do not. We do, however, constantly find ammonia, which, after passing into the blood or lymph, has united with carbonic acid to form either carbonate or carbamate of ammonium. It is quite probable that the nitrogenous waste that leaves the muscles and other tissues is split off from them as ammonia, and not in the shape of large molecules of amino-acid, which are subsequently converted into ammonia. The experiments outside the body which most closely imitate those occurring within the body are those of Drechsel, in which he passed strong alternating currents through solutions of proteid-like materials. Such alternating currents are certainly absent in the body, but their effect, which is a rapidly changing series of small oxidations and reductions, are analogous to metabolic processes; under such circumstances the carbon atoms are burnt off as carbon dioxide, and the nitrogen is split off in the form of ammonia; by the union of these two substances ammonium carbonate is formed.

The following structural formulæ exhibit the relationship between ammonium carbonate, ammonium carbamate, and urea. The loss of one molecule of water from ammonium carbonate produces ammonium carbamate; the loss of a second molecule of water produces urea—



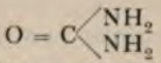
$$O = C\begin{array}{l}\diagup O.NH_4\\ \diagdown O.NH_4\end{array}$$

[Ammonium carbonate.]



$$O = C\begin{array}{l}\diagup NH_2\\ \diagdown O.NH_4\end{array}$$

[Ammonium carbamate.]



$$O = C\begin{array}{l}\diagup NH_2\\ \diagdown NH_2\end{array}$$

[Urea or carbamide.]

Ammonia.

The urine of man and carnivora contains small quantities of ammonium salts. In man the daily amount of ammonia excreted varies between 0·3 and 1·2 grammes; the average is 0·7 gramme. The ingestion of ammonium carbonate does not increase the amount of ammonia in the urine, but increases the amount of urea, into which substance the ammonium carbonate is easily converted. But if a more stable salt, like ammonium chloride, is given, it appears as such in the urine.

Under normal circumstances the amount of ammonia depends on the adjustment between the production of acid substances in metabolism and the supply of bases in the food. Ammonia formation is the physiological remedy for deficiency of bases.

When the production of acids is excessive (as in diabetes), or when mineral acids are given by the mouth or injected into the blood-stream, the result is an increase of the physiological remedy, and excess of ammonia passes over into the urine. Under normal circumstances ammonia is kept at a minimum, being finally converted into the less toxic substance urea, which the kidneys easily excrete. The defence of the organism against acids which are very toxic, is an increase of ammonia formation, or, to put it more correctly, less of the ammonia formed is converted into urea.

Under the opposite conditions, namely, excess of alkali, either in food or given as such, the ammonia disappears from the urine, all being converted into urea. Hence the diminution of ammonia in the urine of man on a vegetable diet, and its absence in the urine of herbivorous animals.

Not only is this the case, but if ammonium chloride is given to a herbivorous animal like a rabbit, the urinary ammonia is but little increased. It reacts with sodium carbonate in the tissues, forming ammonium carbonate (which is excreted as urea) and sodium chloride. Herbivora also suffer much more from, and are more easily killed by, acids than carnivora, their organisation not permitting a ready supply of ammonia to neutralise excess of acids.

Uric Acid.

Uric Acid ($C_5N_4H_4O_3$) is, in mammals, the medium by which a very small quantity of nitrogen is excreted from the body. It is, however, in birds and reptiles the principal nitrogenous constituent of their urine. It is not present in the free state, but is combined with bases to form urates.

It may be obtained from human urine by adding 5 c.c. of hydrochloric acid to 100 c.c. of the urine, and allowing the mixture to stand for twelve to twenty-four hours. The crystals which form are deeply tinged with urinary pigment, and though by repeated solution in caustic soda or potash, and precipitation by hydrochloric acid, they may be obtained fairly free from pigment, pure uric acid is more readily obtained from the solid urine of a serpent or bird, which consists principally of the acid ammonium urate. This is dissolved in soda, and then the addition of hydrochloric acid produces as before the crystallisation of uric acid from the solution.

The pure acid crystallises in colourless rectangular plates or prisms. In striking contrast to urea it is a most insoluble substance, requiring for its solution 1900 parts of hot and 15,000 parts of cold water. The forms which uric acid assumes when precipitated from human urine, either by the addition of hydrochloric acid or in certain pathological processes, are very various, the most frequent being the whetstone shape; there are also bundles of crystals resembling sheaves, barrels, and dumb-bells (see fig. 429).

The *murexide* test is the principal test for uric acid. The test has received the name on account of the resemblance of the colour to the purple of the ancients, which was obtained from certain snails of the genus *Murex*. It is performed as follows: place a little uric acid or a urate in a capsule; add a little dilute nitric acid and evaporate to dryness. A yellowish-red residue is left. Add a little ammonia carefully, and the residue turns violet; this is due to the formation of purpurate of ammonia. On the addition of potash the colour becomes bluer.

Another reaction that uric acid undergoes (though it is not applicable as a test) is, that on treatment with certain oxidising reagents urea and oxalic acid can be obtained from it. Alloxan ($C_4H_2N_2O_4$) or allantoin ($C_4H_6N_4O_3$) are intermediate products. It is, however, doubtful whether a similar oxidation occurs in the normal metabolic processes of the body.

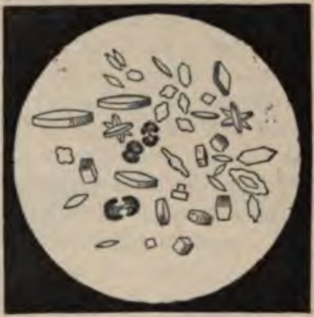


FIG. 429.—Various forms of uric acid crystals.

Uric acid is dibasic, and thus there are two classes of urates—the normal urates and the acid urates. A normal urate is one in which two atoms of the hydrogen are replaced by two of a monad metal like sodium; an acid urate is one in which only one atom of hydrogen is thus replaced. The formulæ would be—

$$\begin{aligned} C_5H_4N_4O_3 &= \text{uric acid.} \\ C_5H_3NaN_4O_3 &= \text{acid sodium urate.} \\ C_5H_2Na_2N_4O_3 &= \text{normal sodium urate.} \end{aligned}$$

The acid sodium urate is the chief constituent of the pinkish deposit of urates, which often occurs in urine, and is called the *lateritious deposit.*

If uric acid is represented by H_2U, the normal urates may be represented by M_2U, and the acid urates by MHU. Bence Jones, and later Sir W. Roberts, considered that the urates actually occurring in urine are what are termed quadriurates $MHU.H_2U$. There is much doubt whether such compounds really exist; if they do, they are readily decomposed into acid urate, MHU, and free uric acid, H_2U.

The quantity of uric acid excreted by an adult varies from 7 to 10 grains (0·5 to 0·75 gramme) daily.

The best method for determining the quantity of uric acid in the urine is that of Hopkins. Ammonium chloride in crystals is added to the urine until no more will dissolve. This saturation completely precipitates all the uric acid in the form of ammonium urate. After standing for two hours the precipitate is collected on a filter, washed with saturated solution of ammonium chloride, and then dissolved in weak alkali. From this solution the uric acid is precipitated by neutralising with hydrochloric acid. The precipitate of uric acid is collected on a weighed filter, dried, and weighed; or the crystals may be dissolved in sodium carbonate solution, and titrated with standard solution of potassium permanganate, until a diffused pink flush appears throughout the solution.

Origin of Uric Acid.—Uric acid is not made by the kidneys. When the kidneys are removed uric acid continues to be formed and accumulates in the organs, especially in the liver and spleen. The liver has been removed from birds, and uric acid is then hardly formed at all, its place being taken by ammonia and lactic acid. It is therefore probable in these animals that ammonia and lactic acid are normally synthesised in the liver to form uric acid.

The chief conditions which lead to an increase of uric acid are:—

1. Increase of meat diet and diminution of oxidation processes, such as occur in people with sedentary habits.

2. Pathological conditions allied to gout.

3. Increase of white corpuscles in the blood, especially in the disease known as *leucocythæmia*. This latter fact is of great interest, as leucocytes contain large quantities of nuclein. Nuclein yields nitrogenous (purine) bases (adenine, hypoxanthine, etc.), which are closely related to uric acid.

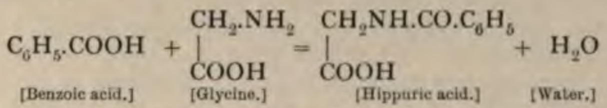
The close relationship of the purine bases to uric acid has been clearly demonstrated by the work of Emil Fischer, for they are all derivatives of the substance called *purine*. The names and formulæ of these substances are as follows:—

	Purine	$C_5H_4N_4$
Purine bases	Hypoxanthine (monoxy-purine)	$C_5H_4N_4O$
	Xanthine (dioxy-purine)	$C_5H_4N_4O_2$
	Adenine (amino-purine)	$C_5H_3N_4.NH_2$
	Guanine (amino-oxy-purine)	$C_5H_3N_4O.NH_2$
	Uric acid (trioxy-purine)	$C_5H_4N_4O_3$

We have here a way in which uric acid may arise by oxidation from the nuclein bases, and thus ultimately from the nuclei of cells. Certain forms of diet increase uric acid formation by leading to an increase of leucocytes and consequently increase in the metabolism of their nuclei; in some cases, however, the increase is chiefly due to nuclein in the food. Uric acid, which comes from nuclein or purine substances in the food, is termed *exogenous*; that which arises from metabolism is termed *endogenous*. Although special attention has been directed to the nuclei of leucocytes because these can be readily examined during life, it must be remembered that the nuclein metabolism of all cells may contribute to uric acid formation. The synthetic formation of uric acid from ammonia and lactic acid, which is so important in birds, occurs in mammals to a slight extent only.

Hippuric Acid.

Hippuric Acid ($C_9H_9NO_3$), combined with bases to form hippurates, is present in small quantities in human urine, but in large quantities in the urine of herbivora. This is due to the food of herbivora containing substances belonging to the aromatic group—the benzoic acid series. If benzoic acid is given to a man, it unites with glycine with the elimination of a molecule of water, and is excreted as hippuric acid—



$$\underset{\text{[Benzoic acid.]}}{C_6H_5.COOH} + \underset{\text{[Glycine.]}}{\begin{matrix} CH_2.NH_2 \\ | \\ COOH \end{matrix}} = \underset{\text{[Hippuric acid.]}}{\begin{matrix} CH_2NH.CO.C_6H_5 \\ | \\ COOH \end{matrix}} + \underset{\text{[Water.]}}{H_2O}$$

This is a well-marked instance of synthesis carried out in the animal body, and experimental investigation shows that it is accomplished by the living cells of the kidney itself; for if a mixture of glycine, benzoic acid, and blood is injected through the kidney (or mixed with a minced kidney just removed from the body of an animal), their place is found to have been taken by hippuric acid.

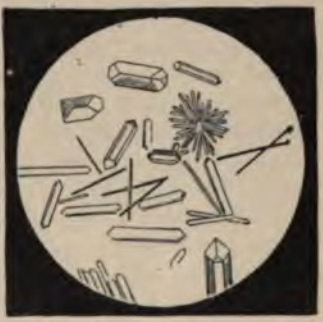


FIG. 430.—Crystals of hippuric acid.

Creatinine.

The **creatinine** of the urine is next to urea its most abundant nitrogenous constituent. Some is derived directly from the creatine of the meat in the food. The remainder is a product of proteid katabolism, and the creatine of the muscles is possibly an intermediate stage in its formation. This amount remains very constant even when the proteid of the food is greatly reduced in quantity. (Folin.)

The formation of creatinine from creatine is represented in the following equation:—

$$\underset{\text{[Creatine.]}}{C_4H_9N_3O_2} - \underset{\text{[Water.]}}{H_2O} = \underset{\text{[Creatinine.]}}{C_4H_7N_3O.}$$

Creatine and creatinine are of considerable chemical interest, because urea can be obtained from them as one of their decomposition products in the laboratory; the equation which represents the formation of urea from creatine is as follows:—

$$\underset{\text{[Creatine.]}}{C_4H_9N_3O_2} + \underset{\text{[Water.]}}{H_2O} = \underset{\text{[Urea.]}}{CON_2H_4} + \underset{\text{[Sarcosine.]}}{C_3H_7NO_2.}$$

The second substance formed is sarcosine. Sarcosine is methylglycine—that is, amino-acetic acid in which one H is replaced by methyl (CH_3)

$$CH_2\begin{matrix} \diagup NH.CH_3 \\ \diagdown COOH. \end{matrix}$$

Creatinine with zinc chloride gives a characteristic crystalline precipitate (groups of fine needles) with composition

$$C_4H_7N_3O.ZnCl_2.$$

According to the recent researches of G. S. Johnson, urinary creatinine, though isomeric with the creatinine obtained artificially from the creatine of flesh, differs from it in some of its properties, such as reducing power, solubility, and character of its gold salts. The reducing action of urinary creatinine has led to some confusion, for some physiologists have supposed that the reducing action on Fehling's solution and picric acid of normal urine is due to sugar, whereas it is really chiefly due to creatinine. The readiest way of separating creatinine from urine is the following:—To the urine a twentieth of its volume of a saturated solution of sodium acetate is added, and then one-fourth of its volume of a saturated solution of mercuric chloride: this produces an immediate abundant precipitate of urates, sulphates, and phosphates, which is removed by filtration; the filtrate is then allowed to stand for twenty-four hours, when the precipitation of a mercury salt of creatinine $(C_4H_5HgN_3OHCl)_4(HgCl_2)_3 + 2H_2O$ occurs in the form of minute spheres, quite typical on microscopic examination. This compound lends itself very well to quantitative analysis. It may be collected, dried, and weighed, and one-fifth of the weight found is creatinine. Creatinine may be obtained from it by suspending it in water, decomposing it with sulphuretted hydrogen, and filtering. The filtrate deposits creatinine hydrochloride, from which lead hydrate liberates creatinine. An important point in Johnson's process is that all the operations are carried out in the cold; if heat is applied one obtains the creatinine of former writers, which has no reducing power.

The Inorganic Constituents of Urine.

The inorganic or mineral constituents of urine are chiefly chlorides, phosphates, sulphates, and carbonates; the metals with which these are in combination are sodium, potassium, ammonium, calcium, and magnesium. The total amount of these salts varies from 19 to 25 grammes daily. The most abundant is sodium chloride, which averages in amount 10 to 16 grammes per diem. These substances are derived from two sources—first from the food, and secondly as the result of metabolic processes. The chlorides and most of the phosphates come from the food; the sulphates and some of the phosphates, as a result of metabolism. The salts of the blood and of the urine are much the same, with the important exception that, whereas the blood contains only traces of sulphates, the urine contains abundance of these salts. The sulphates are derived from the changes that occur in the proteids of the body; the nitrogen of proteids leaves the body as urea and uric acid; the sulphur of the proteids is oxidised to form sulphuric acid, which passes into the urine in the form of sulphates. The excretion of sulphates, moreover, though it occurs earlier than that of urea, runs parallel with it.

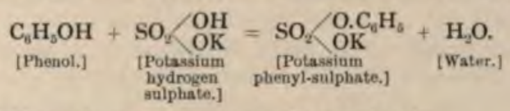
Chlorides.—The chief chloride is that of sodium. The ingestion of sodium chloride is followed by its appearance in the urine, some on the same day, some on the next day. Some is decomposed to form the hydrochloric acid of the gastric juice. The salt, in passing through the body, fulfils the useful office of stimulating metabolism and secretion.

Sulphates.—The sulphates in the urine are principally those of potassium and sodium. They are derived from the metabolism of proteids in the body. Only the smallest trace enters the body with the food. Sulphates have an unpleasant bitter taste (for instance, Epsom salts): hence we do not take food that contains them. The sulphates vary in amount from 1·5 to 3 grammes daily.

In addition to these sulphates there is a small quantity, about one-tenth of the total sulphates, that are combined with organic radicles: these are known as ethereal sulphates, and they originate from putrefactive processes occurring in the intestine. The chief of these ethereal sulphates are phenyl sulphate of potassium and indoxyl sulphate of potassium. The latter originates from the indole formed in the intestine, and as it yields indigo when treated with certain reagents it is sometimes called *indican*. It is very important to remember that the indican of urine is not the same thing as the indican of plants, which is a glucoside. Both yield indigo, but there the resemblance ceases.

The formation of these sulphates is somewhat important; the aromatic substances liberated by putrefactive processes in the intestine are poisonous, but their conversion into ethereal sulphates renders them harmless.

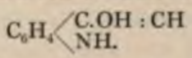
The equation representing the formation of potassium phenyl-sulphate is as follows :—



$$C_6H_5OH + SO_2{<}\begin{matrix}OH\\OK\end{matrix} = SO_2{<}\begin{matrix}O.C_6H_5\\OK\end{matrix} + H_2O.$$

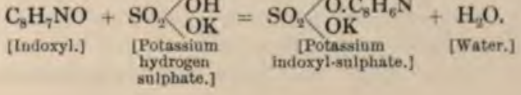
[Phenol.] [Potassium hydrogen sulphate.] [Potassium phenyl-sulphate.] [Water.]

Indole (C_8H_7N) on absorption is converted into indoxyl :—



$$C_6H_4{<}\begin{matrix}C.OH : CH\\NH.\end{matrix}$$

The equation representing the formation of potassium indoxyl-sulphate is as follows :—



$$C_8H_7NO + SO_2{<}\begin{matrix}OH\\OK\end{matrix} = SO_2{<}\begin{matrix}O.C_8H_6N\\OK\end{matrix} + H_2O.$$

[Indoxyl.] [Potassium hydrogen sulphate.] [Potassium indoxyl-sulphate.] [Water.]

Carbonates.—Carbonates and bicarbonates of sodium, calcium, magnesium, and ammonium are only present in alkaline urine. They arise from the carbonates of the food, or from vegetable acids (malic, tartaric, etc.) in the food. They are, therefore, found in the urine of herbivora and vegetarians, whose urine is thus rendered alkaline. Urine containing carbonates becomes, like saliva, cloudy on standing, the precipitate consisting of calcium carbonate, and also phosphates.

Phosphates.—Two classes of phosphates occur in normal urine:—

(1) Alkaline phosphates—that is, phosphates of sodium (abundant) and potassium (scanty).

(2) Earthy phosphates—that is, phosphates of calcium (abundant) and magnesium (scanty).

The composition of the phosphates in urine is liable to variation.

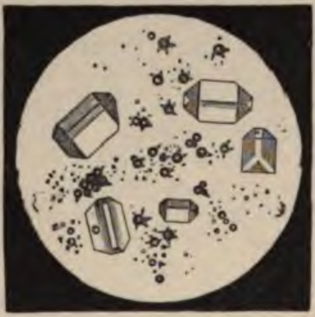


FIG. 431.—Urinary sediment of triple phosphates (large prismatic crystals) and urate of ammonium, from urine which had undergone alkaline fermentation.

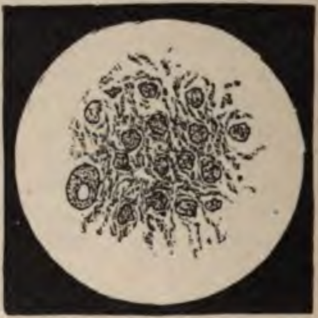


FIG. 432.—Mucus deposited from urine.

In acid urine the acidity is due to the acid salts. These are chiefly:—

Sodium dihydrogen phosphate, NaH_2PO_4, and calcium dihydrogen phosphate, $Ca(H_2PO_4)_2$.

In neutral urine, in addition, disodium hydrogen phosphate (Na_2HPO_4), calcium hydrogen phosphate, $CaHPO_4$, and magnesium hydrogen phosphate, $MgHPO_4$, are found. In alkaline urine there may be instead of, or in addition to, the above, the normal phosphates of sodium, calcium, and magnesium [Na_3PO_4, $Ca_3(PO_4)_2$, $Mg_3(PO_4)_2$].

The earthy phosphates are precipitated by rendering the urine alkaline by ammonia. In decomposing urine, ammonia is formed from the urea: this also precipitates the earthy phosphates. The phosphates most frequently found in the white creamy precipitate which occurs in decomposing urine are:—

(1) Triple phosphate or ammonio-magnesium phosphate

($NH_4MgPO_4 + 6H_2O$). This crystallises in "coffin-lid" crystals (see fig. 431) or feathery stars.

(2) Stellar phosphate, or calcium phosphate; this crystallises in star-like clusters of prisms.

As a rule normal urine gives no precipitate when it is boiled; but sometimes neutral, alkaline, and occasionally faintly acid urines give a precipitate of calcium phosphate when boiled: this precipitate is amorphous, and is liable to be mistaken for albumin. It may be distinguished readily from albumin, as it is soluble in a few drops of acetic acid, whereas coagulated proteid does not dissolve.

The phosphoric acid in the urine chiefly originates from the phosphates of the food, but is partly a decomposition product of the phosphorised organic materials in the body, such as lecithin and nuclein. The amount of P_2O_5 in the twenty-four hours' urine varies from 2·5 to 3·5 grammes, of which the earthy phosphates contain about half (1 to 1·5 gr.).

Tests for the Inorganic Salts of Urine.

Chlorides.—Acidulate with nitric acid and add silver nitrate; a white precipitate of silver chloride, soluble in ammonia, is produced. The object of acidulating with nitric acid is to prevent phosphates being precipitated by the silver nitrate.

Sulphates.—Acidulate with hydrochloric acid, and add barium chloride. A white precipitate of barium sulphate is produced. Hydrochloric acid is again added first, to prevent precipitation of phosphates.

Phosphates.—i. Add ammonia; a white crystalline precipitate of earthy (that is, calcium and magnesium) phosphates is produced. This becomes more apparent on standing. The alkaline (that is, sodium and potassium) phosphates remain in solution. ii. Mix another portion of urine with half its volume of nitric acid; add ammonium molybdate, and boil. A yellow crystalline precipitate falls. This test is given by both classes of phosphates.

Quantitative estimation of the salts is accomplished by the use of solutions of standard strength, which are run into the urine till the formation of a precipitate ceases. The standards are made of silver nitrate, barium chloride, and uranium nitrate or acetate for chlorides, sulphates and phosphates respectively.

Urinary Deposits.

The different substances that may occur in urinary deposits are formed elements and chemical substances.

The **formed** or **anatomical elements** may consist of blood corpuscles, pus, mucus, epithelium cells, spermatozoa, casts of the urinary tubules, fungi, and entozoa. All of these, with the exception of a small quantity of mucus, which forms a flocculent cloud in the urine, are pathological, and the microscope is chiefly employed in their detection.

The **chemical substances** are uric acid, urates, calcium oxalate, calcium carbonate, and phosphates. Rarer forms are leucine, tyrosine, xanthine, and cystin. We shall, however, here only consider the commoner deposits, and for their identification the microscope and chemical tests must both be employed.

Deposit of Uric Acid.—This is a sandy reddish deposit resembling cayenne pepper. It may be recognised by its crystalline form (fig. 429, p. 561) and the murexide reaction. The presence of these crystals generally indicates an increased formation of uric acid, and, if excessive, may lead to the formation of stones or calculi in the bladder.

Deposit of Urates.—This is much commoner, and may, if the urine is concentrated, occur in normal urine when it cools. It is generally found in the concentrated urine of fevers; and there appears to be a kind of fermentation, called the acid fermentation, which occurs in the urine after it has been passed, and which leads to the same result. The chief constituent of the deposit is the acid sodium urate, the formation of which from the normal sodium urate of the urine may be represented by the equation:—

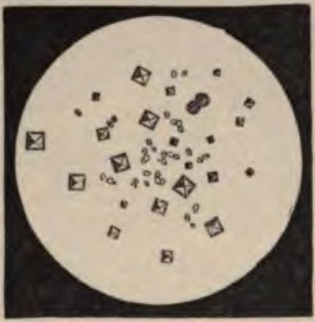


Fig. 433.—Crystals of calcium oxalate.

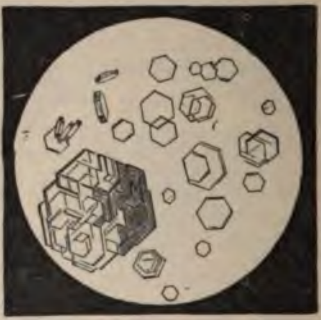


Fig. 434.—Crystals of cystin.

$$\underset{\text{[Normal sodium urate.]}}{2C_5H_2Na_2N_4O_3} + \underset{\text{[Water.]}}{H_2O} + \underset{\text{[Carbonic acid.]}}{CO_2} = \underset{\text{[Acid sodium urate.]}}{2C_5H_3NaN_4O_3} + \underset{\text{[Sodium carbonate.]}}{Na_2CO_3}.$$

This deposit may be recognised as follows:—

(1) It has a pinkish colour; the pigment called *uro-erythrin* is one of the pigments of the urine, but its relationship to the other urinary pigments is not known.

(2) It dissolves upon warming the urine.

(3) Microscopically it is usually amorphous, but crystalline forms similar to those depicted in fig. 431 may occur. Crystals of calcium oxalate may be mixed with this deposit (see fig. 433).

Deposit of Calcium Oxalate.—This occurs in envelope crystals (octahedra) or dumb-bells. It is insoluble in ammonia, and in acetic acid. It is soluble with difficulty in hydrochloric acid.

Deposit of Cystin.—Cystin ($C_6H_{12}N_2S_2O_4$) is recognised by its colourless six-sided crystals (fig. 434). These are rare: they occur only in acid urine, and they may form concretions or calculi. Cystinuria (cystin in the urine) is hereditary.

Deposit of Phosphates.—These occur in alkaline urine. The urine may be alkaline when passed, due to fermentative changes occurring in the bladder. All urine, however, if exposed to the air (unless the air is perfectly pure, as on the top of a snow mountain), will in time become alkaline, owing to the growth of the *micrococcus ureæ*. This forms ammonium carbonate from the urea.

$$\underset{\text{[Urea.]}}{CON_2H_4} + \underset{\text{[Water.]}}{2H_2O} = \underset{\text{[Ammonium carbonate.]}}{(NH_4)_2CO_3}.$$

The ammonia renders the urine alkaline and precipitates the earthy phosphates. The chief forms of phosphates that occur in urinary deposits are—

(1) Calcium phosphate, $Ca_3(PO_4)_2$; amorphous.

(2) Triple or ammonio-magnesium phosphate, $MgNH_4PO_4$; coffin-lids and feathery stars (fig. 431).

(3) Crystalline phosphate of calcium, $CaHPO_4$, in rosettes of prisms, in spherules, or in dumb-bells.

(4) Magnesium phosphate, $Mg_3(PO_4)_2+22H_2O$, occurs occasionally, and crystallises in long plates.

All these phosphates are dissolved by acids, such as acetic acid, without effervescence.

A solution of ammonium carbonate (1 in 5) eats magnesium phosphate away at the edges; it has no effect on the triple phosphate. A phosphate of calcium ($CaHPO_4+2H_2O$) may occasionally be deposited in acid urine. Pus in urine is apt to be mistaken for phosphates, but can be distinguished by the microscope.

Deposit of calcium carbonate, $CaCO_3$, appears but rarely as whitish balls or biscuit-shaped bodies. It is commoner in the urine of herbivora. It dissolves in acetic or hydrochloric acid, with effervescence.

The following is a summary of the chemical sediments that may occur in urine:—

CHEMICAL SEDIMENTS IN URINE.

IN ACID URINE.	IN ALKALINE URINE.
Uric Acid.—Whetstone, dumb-bell, or sheaf-like aggregations of crystals deeply tinged by pigment. *Urates.*—Generally amorphous. The acid urate of sodium and of ammonium may sometimes occur in star-shaped clusters of needles or spheroidal clumps with projecting spines. Tinged brick-red. Soluble on warming. *Calcium Oxalate.* — Octahedra, so-	*Phosphates.* — Calcium phosphate, $Ca_3(PO_4)_2$. Amorphous. Triple phosphate, $MgNH_4PO_4 + 6H_2O$. Coffin-lids or feathery stars. Calcium hydrogen phosphate, $CaHPO_4$. Rosettes, spherules, or dumb-bells. Magnesium phosphate, $Mg_3(PO_4)_2 + 22H_2O$. Long plates.

CHEMICAL SEDIMENTS IN URINE—*Continued.*

IN ACID URINE.	IN ALKALINE URINE.
called envelope crystals. Insoluble in acetic acid. *Cystin.*—Hexagonal plates. Rare. *Leucine and Tyrosine.*—Rare. *Calcium Phosphate*, $CaHPO_4 + 2H_2O$.—Rare.	All the preceding are soluble in acetic acid without effervescence. *Calcium Carbonate*, $CaCO_3$.—Biscuit-shaped crystals. Soluble in acetic acid with effervescence. *Ammonium Urate*, $C_5H_2(NH_4)_2.N_4O_3$. — "Thorn - apple" spherules. *Leucine and Tyrosine.*—Very rare.

PATHOLOGICAL URINE.

Under this head we shall briefly consider only those abnormal constituents which are most frequently met with.

Proteids.—There is no proteid matter in normal urine,* and the most common cause of the appearance of albumin in the urine is disease of the kidney (Bright's disease). The term "albumin" is the one used by clinical observers. Properly speaking, it is a mixture of serum albumin and serum globulin. Of these, serum albumin is usually the more abundant. Globulins, and especially englobulins, have probably larger molecules, so escape of globulin indicates more serious damage to the renal cells. The best methods of testing for and estimating the proteid are the following:—

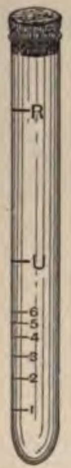


FIG. 435.—Esbach's Albuminometer.

(*a*) Boil the top of a long column of urine in a test-tube. If the urine is acid, the albumin is coagulated. If the quantity of albumin is small, the cloudiness produced is readily seen, as the unboiled urine below it is clear. This is insoluble in a few drops of acetic acid, and so may be distinguished from phosphates. If the urine is alkaline, it should be first rendered acid with a little dilute acetic acid.

(*b*) *Heller's Nitric-acid Test.*—Pour some of the urine gently on to the surface of some nitric acid in a test-tube. A ring of white precipitate occurs at the junction of the two liquids. This test is used for small quantities of albumin.

(*c*) *Estimation of Albumin by Esbach's Albuminometer.*—Esbach's reagent for precipitating the albumin is made by dissolving 10 grammes of picric acid and 20 grammes of citric acid in 800 or 900 c.c. of boiling water, and then adding sufficient water to make up to a litre (1000 c.c.).

The albuminometer is a test-tube graduated as shown in fig. 435.

Pour the urine into the tube up to the mark U; then the reagent up to the mark R. Close the tube with a cork, and to ensure complete mixture, tilt it to and fro a dozen times without shaking. Allow the corked tube to stand upright twenty-four hours; then read off on the scale the height of the coagulum. The figures indicate grammes of dried albumin in a litre of urine. The percentage is obtained by dividing by 10. Thus, if the coagulum stands at 3, the amount of albumin is 3 grammes per litre, or 0·3 gr. in 100 c.c. If the sediment falls between any two figures, the distance ¼, ½, or ¾ from the upper or lower figure can be read off with sufficient accuracy. Thus, the surface of the sediment being midway between 3 and 4 would be read as 3·5. When the albumin is so abundant that the sediment is above 4, a more accurate result is obtained by first diluting the urine with one or two volumes of water, and then multiplying the resulting figure by 2 or 3, as the case may be. If the amount of albumin is less than ·05 per cent., it cannot be accurately estimated by this method.

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* This absolute statement is true for all practical purposes. Mörner, however, has stated that a trace of proteid matter (serum albumin *plus* the proteid constituent of mucin) does occur in normal urine; but the trace is negligible, many hundreds of litres of urine having to be used to obtain an appreciable quantity.

A condition called "peptonuria," or peptone in the urine, is observed in certain pathological states, especially in diseases where there is a formation of pus, and particularly if the pus is decomposed owing to the action of a bacterial growth called staphylococcus; one of the products of disintegration of pus cells appears to be peptone; and this leaves the body by the urine. The term "peptone," however, is in the strict sense of the word incorrect; the proteid present is deutero-proteose. In the disease of bone called "osteomalacia" a proteose is also usually found in the urine. This more nearly resembles hetero-proteose in its properties.

Sugar.—Normal urine contains no sugar, or so little that for clinical purposes it may be considered absent. It occurs in the disease called diabetes mellitus, which can be artificially produced by puncture of the medulla oblongata, or by extirpation of the pancreas. The disease as it occurs in man may be due to disordered metabolism of the liver, to disease of the pancreas, and to other not fully understood causes (see p. 516).

The sugar present is dextrose. Lactose may occur in the urine of nursing mothers. Diabetic urine also contains hydroxybutyric acid, and may contain or yield on distillation acetone, and ethyl-diacetic acid. The methods usually adopted for detecting and estimating the sugar are as follows:—

(*a*) The urine has generally a high specific gravity.

(*b*) The presence of sugar is shown by the reduction (yellow precipitate of cuprous oxide) that occurs on boiling with Fehling's solution. Fehling's solution is an alkaline solution of copper sulphate to which Rochelle salt has been added. The Rochelle salt (double tartrate of potash and soda) holds the cupric hydrate in solution. Fehling's solution should always be freshly prepared, as, on standing, an isomeride is formed from the tartaric acid, which reduces the cupric to cuprous oxide. Fehling's solution should, therefore, always be tested by boiling before it is used. If it remains clear on boiling, it is in good condition.

(*c*) *Picric Acid Test.*—Take a drachm (about 4 c.c.) of diabetic urine; add to it an equal volume of saturated aqueous solution of picric acid, and half the volume (*i.e.*, 2 c.c.) of the liquor potassæ of the British Pharmacopœia. Boil the mixture for about a minute, and it becomes so intensely dark red as to be opaque. Now do the same experiment with normal urine. An orange-red colour appears even in the cold, and is deepened by boiling, but it never becomes opaque, and so the urine for clinical purposes may be considered free from sugar. This reduction of picric acid by normal urine is due to creatinine (see p. 564).

(*d*) *Quantitative Determination of Sugar in Urine.*—Fehling's solution is prepared as follows:—34·639 grammes of copper sulphate are dissolved in about 200 c.c. of distilled water; 173 grammes of Rochelle salt are dissolved in 600 c.c. of a 14 per cent. solution of caustic soda. The two solutions are mixed and diluted to a litre. Ten c.c. of this solution are equivalent to 0·05 gramme of dextrose. Dilute 10 c.c. of this solution with about 40 c.c. of water, and boil it in a porcelain basin. Run into this from a burette the urine (which should be previously diluted with nine times its volume of distilled water) until the blue colour of the copper solution disappears—that is, till all the cupric hydrate is reduced. The mixture in the basin should be boiled after every addition. The quantity of diluted urine used from the burette contains 0·05 gramme of sugar. Calculate the percentage from this, remembering that the urine has been diluted to ten times its original volume.

Pavy's modification of Fehling's solution is often used. Here ammonia holds the copper in solution, and no precipitate forms on boiling with sugar, as ammonia holds the cuprous oxide in solution. The reduction is complete when the blue colour disappears; 10 c.c. of Pavy's solution = 1 c.c. of Fehling's solution = 0·005 gramme of dextrose.

In some cases of diabetic urine where there is excess of ammonio-magnesic phosphate, the full reduction is not obtained with Fehling's solution, and when the quantity of sugar is small it may be missed. In such a case excess of soda or potash should be first added, the precipitated phosphates filtered off, and the filtrate after it has been well boiled may then be titrated with Fehling's solution.

Fehling's test is not absolutely trustworthy. Often a normal urine will decolorise Fehling's solution, though seldom a red precipitate is formed. This is due to excess of urates and creatinine. Another substance called glycuronic acid ($C_6H_{10}O_7$) is, however, very likely to be confused with sugar by Fehling's test; the cause of its appearance is sometimes the administration of drugs (chloral, camphor, etc.); but sometimes it appears independently of drug treatment. (See p. 517.)

In the rare and hereditary condition called alcaptonuria, confusion may also arise. Alcapton is a substance which originates from tyrosine by an unusual form of metabolism. It gives the urine a brown tint, which darkens on exposure to the air. It is an aromatic substance, which Baumann and Wolkow and later Garrod identified with homogentisinic acid ($C_6H_3.(OH)_2CH_2.COOH$).

(*e*) A good confirmatory test for sugar is the *fermentation test*, which is performed as follows:—

Half fill a test-tube with the urine and add a little German yeast. Fill up the tube with mercury; invert it in a basin of mercury, and leave it in a warm place for twenty-four hours. The sugar will undergo fermentation: carbonic acid gas accumulates in the tube, and the liquid no longer gives the tests for sugar, or only faintly, but gives those for alcohol instead. The specific gravity falls. A control experiment should be made with yeast and water in another test-tube, as a small yield of carbonic acid is sometimes obtained from impurities in the yeast.

(*f*) The *phenylhydrazine* test (p. 391) may also be applied.

Bile.—This occurs in jaundice. The urine is dark-brown, greenish, or in extreme cases almost black in colour. The most readily applied test is Gmelin's test for the bile pigments. Pettenkofer's test for the bile acids seldom succeeds in urine if the test is done in the ordinary way. The best method is to warm a thin film of urine and cane sugar solution in a flat porcelain dish. Then dip a glass rod in strong sulphuric acid, and draw it across the film. Its track is marked by a purplish line. Excess of urobilin should not be mistaken for bile pigment.

Blood.—When hæmorrhage occurs in any part of the urinary tract, blood appears in the urine. It is found in the acute stage of Bright's disease. If a large quantity is present, the urine is deep red. Microscopic examination then reveals the presence of blood corpuscles, and on spectroscopic examination the bands of oxyhæmoglobin are seen.

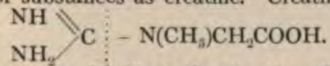
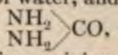
If only a small quantity of blood is present, the secretion—especially if acid—has a characteristic reddish-brown colour, which physicians term "smoky."

The blood pigment may, under certain circumstances, appear in the urine without the presence of any blood corpuscles at all. This is produced by a disintegration of the corpuscles occurring in the circulation, and the most frequent cause of this is a tropical disease allied to ague, which is called *paroxysmal hæmoglobinuria* (Blackwater fever). The pigment is in the condition of methæmoglobin mixed with more or less oxyhæmoglobin, and the spectroscope is the means used for identifying these substances.

Pus occurs in the urine as the result of suppuration in any part of the urinary tract. It forms a white sediment resembling that of phosphates, and, indeed, is always mixed with phosphates. The pus corpuscles may, however, be seen with the microscope; their nuclei are rendered evident by treatment with 1 per cent. acetic acid, and the pus corpuscles are seen to resemble white blood-corpuscles, which, in fact, they are in origin. They dissolve in glacial acetic acid.

Some of the proteid constituents of the pus cells—and the same is true for blood—pass into solution in the urine, so that the urine pipetted off from the surface of the deposit gives the tests for albumin.

On the addition of liquor potassæ to the deposit of pus cells, a ropy gelatinous mass is obtained. This is distinctive. Mucus treated in the same way is dissolved.

Arginine and Arginase. We have seen (p. 557) that arginine belongs to the same class of substances as creatine. Creatine (methyl-guanidine-acetic acid) has the formula  $\left.\begin{matrix}NH\\NH_2\end{matrix}\right>C\ \vdots - N(CH_3)CH_2COOH$. On decomposition this takes up a molecule of water, and splits in the situation of the dotted line in the above formula into urea  $\left.\begin{matrix}NH_2\\NH_2\end{matrix}\right>CO$, and sarcosine $NH(CH_3)CH_2COOH$ (see also p. 563). The formula for arginine differs from that of creatine on the right-hand side of the formula, where the sarcosine group is replaced by that of diamino-valeric acid or ornithine. The decomposition of arginine into urea and ornithine can be brought about by a ferment called *arginase* (Kossel and Dakin) which occurs in the tissues, especially in the liver. This is the first discovery of a urea-forming ferment.

CHAPTER XXXVIII

THE SKIN AND ITS APPENDAGES

THE skin is composed of two parts, *epidermis* or *cuticle*, and *dermis* or *cutis vera*.

The Epidermis is composed of a large number of layers of cells; it is a very thick stratified epithelium. The deeper layers are protoplasmic, and form the *rete mucosum*, or *Malpighian layer;* the surface layers are hard and horny; this horny layer is the thickest part of the epidermis, and is specially thick on the palms and soles, where

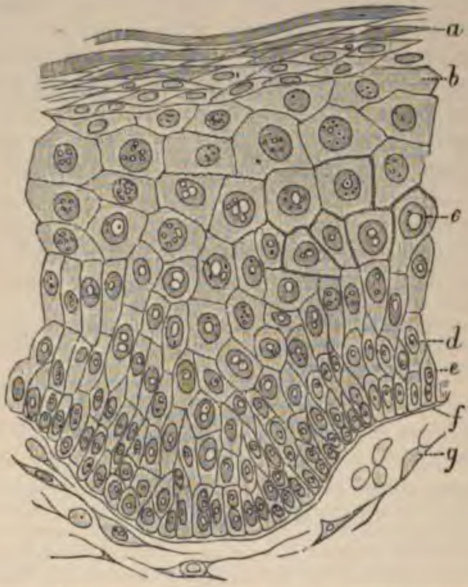


FIG. 436.—Vertical section of the epidermis of the prepuce. *a*, stratum corneum, of very few layers the stratum lucidum and stratum granulosum not being distinctly represented; *b*, *c*, *d*, and *e*, the layers of the stratum Malpighii, a certain number of the cells in layers *d* and *e* showing signs of division; it consists chiefly of prickle cells; *g*, connective-tissue cells in cutis vera. (Cadiat.)

it is subjected to most friction. The cells of the deepest layers of the Malpighian layer are columnar in shape; the layers next to these are composed of polyhedral cells, which become flatter as they approach the horny layers. Between these cells are fine intercellular passages, bridged across by fine protoplasmic processes, which pass from cell to cell; the spaces between the cells serve for the passage of lymph. It is in the cells of the Malpighian layer that pigment granules are deposited in the coloured races.

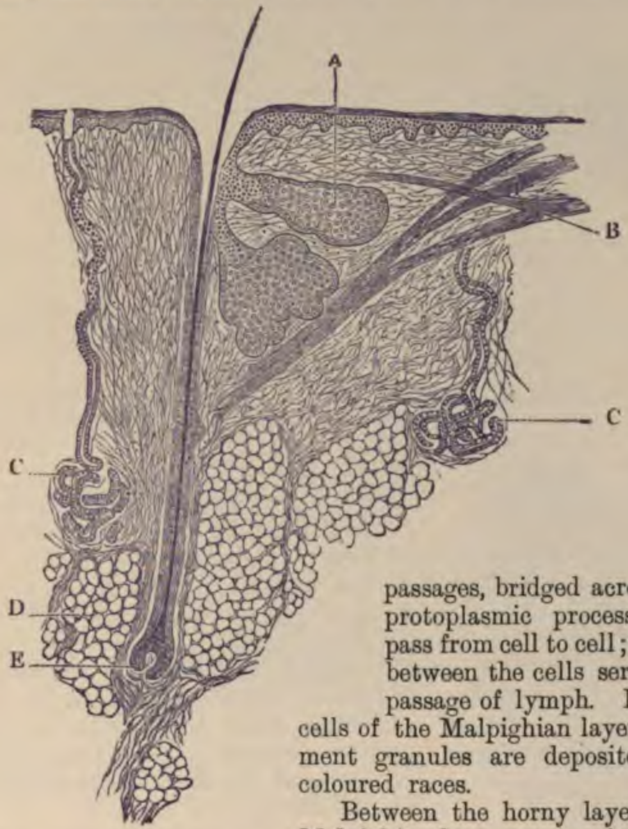


FIG. 437.—Vertical section of skin. A. Sebaceous gland opening into hair follicle. B. Muscular fibres. C. Sudoriferous or sweat-gland. D. Subcutaneous fat. E. Fundus of hair follicle, with hair papilla. (Klein.)

Between the horny layer and the Malpighian layer are two intermediate strata, in which the transformation of protoplasm into horny material (*keratin*) is taking place. In the first of these—that is, the one next to the Malpighian layer, the cells are flattened, and filled with large granules of *eleidin*, an intermediate substance in the formation of horn. This layer is called the *stratum granulosum.*

Above this are several layers of clear, more rounded cells, which constitute the *stratum lucidum;* and above this the horny layer proper, many strata deep, begins. The cells become more and more scaly as they approach the surface, where they lose their nuclei and eventually become detached.

The epidermis grows by a multiplication of the deepest layer of cells (fig. 436 *e*); the newly-formed cells push towards the surface those previously formed, in their progress undergoing the transformation into keratin.

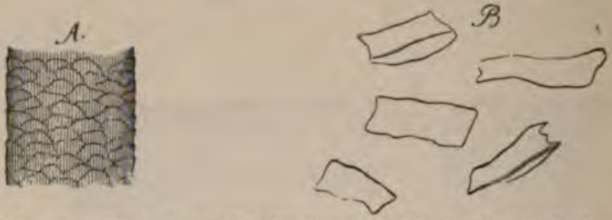


FIG. 438.—Surface of a white hair, magnified 160 diameters. The wavy lines mark the upper or free edges of the cortical scales. *B*, separated scales, magnified 350 diameters. (Kölliker.)

The epidermis has no blood-vessels; nerve-fibrils pass into its deepest layers, and ramify between the cells.

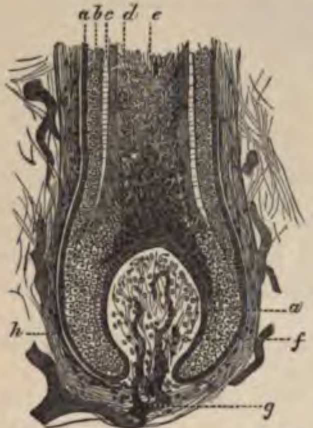


FIG. 439.—Longitudinal section of a hair follicle. *a* and *b*, external root-sheath; *c*, internal root-sheath; *d*, fibrous layer of the hair; *e*, medulla; *f*, hair papilla; *g*, blood-vessels of the hair papilla; *h*, dermic coat. (Cadiat.)

The Dermis is composed of dense fibrous tissue, which becomes looser and more reticular in its deeper part, where it passes by insensible degrees into the areolar and adipose tissue of the subcutaneous region. The denser superficial layer is very vascular, and is covered with minute *papillæ;* the epidermis is moulded over these, and in the palms and soles, where the papillæ are largest and are disposed in rows, their presence is indicated by the well-known ridges on the surface.

The papillæ contain loops of capillaries, and in some cases, especially in the palm of the hand and fingers, they contain tactile corpuscles (which will be more fully described in connection with the sense of touch). Special capillary networks are distributed to the sweat-glands, sebaceous glands, and hair follicles.

The deeper portions of the dermis in the scrotum, penis, and nipple, contain involuntary muscular tissue; there is also a bundle of muscular tissue attached to each hair follicle.

The Nails are thickenings of the stratum lucidum. Each lies in a depression called the *bed* of the nail, the posterior part of which is overlapped by epidermis, and called the *nail-groove.* The dermis beneath is beset with longitudinal ridges instead of papillæ; these are very vascular; but in the *lunula,* the crescent at the base of the nail, there are papillæ, and this part is not so vascular.

The Hairs are epidermal growths, contained in pits called *hair follicles.* The part within the follicle is called the *root* of the hair.

The main substance of the hair is composed of pigmented horny fibrous material, in reality long fibrillated cells. It is covered by a layer of scales imbricated upwards (*hair cuticle*). In many hairs the centre is occupied by a *medulla,* formed of rounded cells containing eleidin granules. Minute air-bubbles may be present in both medulla and fibrous layer, and cause the hair to look white by reflected light. The grey hair of old age, however, is produced by a loss of pigment.

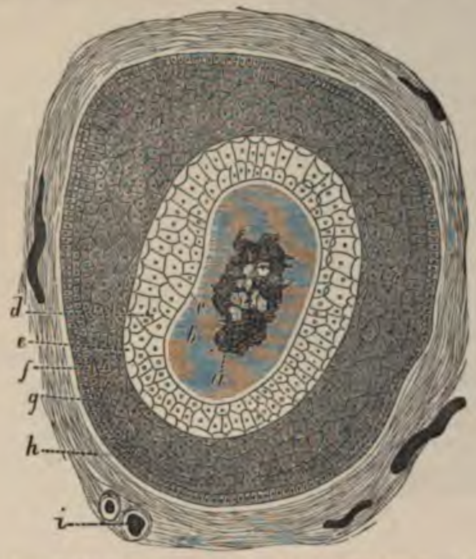


FIG. 440.—Transverse section of a hair and hair follicle made below the opening of the sebaceous gland. *a*, medulla, or pith of the hair; *b*, fibrous layer; *c*, cuticle; *d*, Huxley's layer; *e*, Henle's layer of internal root-sheath; *f* and *g*, layers of external root-sheath, outside of *g* is the basement membrane or hyaline layer; *h*, dermic (fibrous) coat of hair follicle; *i*, vessels. (Cadiat.)

The root is enlarged at its extremity into a *knob,* into which projects a vascular *papilla* from the true skin.

The hair follicle consists of two parts, one continuous with the epidermis, called the *root-sheath,* the other continuous with the dermis, called the *dermic coat.* The two are separated by a basement membrane called the *hyaline layer* of the follicle. The root-sheath consists of an outer layer of cells like the Malpighian layer of the epidermis, with which it is directly continuous (*outer root-sheath*), and of an inner horny layer (*inner root-sheath*), continuous with the horny layer of the epidermis. The inner root-sheath consists of three layers, the outermost being composed of long, non-nucleated cells (*Henle's layer*), the next of squarish nucleated cells (*Huxley's layer*), and the third is a *cuticle* of scales, imbricated downwards, which fit over the scales of the cuticle of the hair itself.

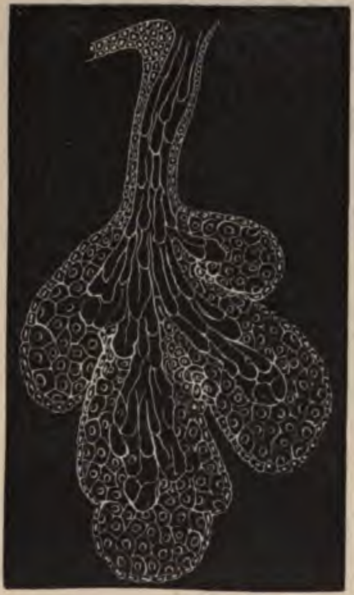


FIG. 441.—Sebaceous gland from human skin. (Klein and Noble Smith.)

A small bundle of plain muscular fibres is attached to each follicle (fig. 437). When it contracts, as under the influence of cold, or of certain emotions such as fear, the hair is erected and the whole skin is roughened ("goose skin"). The nerves supplying these muscles are called *pilo-motor* nerves. The distribution of these nerves closely follows those of the vaso-constrictor nerves of the skin; their cell stations are in the lateral sympathetic chain.

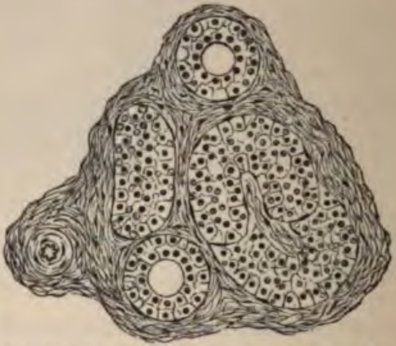


FIG. 442.—Terminal tubules of sudoriferous or sweat-glands, cut in various directions from the skin of the pig's ear. (V. D. Harris.)

The sebaceous glands (figs. 437 and 441) are small saccular glands, with ducts opening into the upper portion of the hair follicles. The secreting cells become charged with fatty matter, which is discharged into the lumen of the saccules owing to the disintegration of the cells. The secretion, *sebum*, contains isocholesterin (see p. 512) in addition to fatty matter. It acts as a lubricant to the hairs.

The sweat-glands are abundant over the whole human skin, but are most numerous where hairs are absent, on the palms and soles. Each consists of a coiled tube in the deepest part of the dermis, the duct from which passes up through the dermis, and by a corkscrew-like canal through the epidermis to the surface.

The secreting tube is lined by one or two layers of cubical or columnar cells; outside this is a layer of longitudinally arranged muscular fibres, and then a basement-membrane.

The duct is of similar structure, except that there is usually but one layer of cubical cells, and muscular fibres are absent; the passage through the epidermis has no proper wall; it is merely a channel excavated between the epidermal cells.

The ceruminous glands of the ear are modified sweat-glands.

THE FUNCTIONS OF THE SKIN

Protection.—The skin acts as a protective organ, not only by mechanically covering and so defending internal structures from external violence, but more particularly in virtue of its being an organ of **sensation** (see later in the chapter on Touch).

Heat Regulation.—See Chapter XL.

Respiration.—A small amount of respiratory interchange of gases occurs through the skin, but in thick-skinned animals this is very small. In man, the carbonic acid exhaled by the skin is about $\frac{1}{150}$ to $\frac{1}{200}$ of that which passes from the lungs. But in thin-skinned animals, like frogs, cutaneous respiration is very important; after the removal of the lungs of a frog, the respiratory interchange through the skin is sufficient to keep the animal alive, the amount of carbonic acid formed being about half as much as when the lungs are present (Bischoff).

Absorption.—This also is an unimportant function; but the skin will in a small measure absorb oily materials placed in contact with it; thus in some cases infants who will not take cod-liver oil by the mouth, can yet be dosed with it by rubbing it into the skin. Many ointments also are absorbed, and thus general effects produced by local inunction.

Secretion.—The secretions of the skin are two in number. The *sebum* is the natural lubricant of the hairs. The secretion of sweat is an important function of the skin, and we will therefore discuss it at greater length.

THE SWEAT

Physiology of the Secretion of Sweat.—We have seen that the sweat-glands are most abundant in man on the palms and soles, and here the greatest amount of perspiration occurs. Different animals vary a good deal in the amount of sweat they secrete, and in the place where the secretion is most abundant. Thus the ox perspires less than the horse and sheep; perspiration is absent from rats, rabbits, and goats; pigs perspire mostly on the snout; dogs and cats on the pads of the feet.

As long as the secretion is small in amount, it is evaporated from the surface at once; this is called *insensible perspiration.* As soon as the secretion is increased or evaporation prevented, drops appear on the surface of the skin. This is known as *sensible perspiration.* The relation of these two varies with the temperature of the air; the drier and hotter the air, the greater being the proportion of insensible to sensible perspiration. In round numbers the total amount of sweat secreted by a man is two pounds in the twenty-four hours.

The amount of secretion is influenced by the vaso-motor nerves; an increase in the size of the skin-vessels leads to increased, a constriction of the vessels to diminished, perspiration. There are also special secretory fibres, stimulation of which causes a secretion even when the circulation is suspended, as in a recently amputated limb. These fibres are paralysed by atropine. They are contained in the same nerve-trunks as the vaso-motor nerves, as are also the nerve-fibres which supply the plain muscular fibres of the sweat-glands which act during the expulsion of the secretion. The secretory nerves for the lower limbs issue from the spinal cord by the last two or three dorsal and first two or four lumbar nerves (in the cat); they have cell stations in the lower ganglia of the lateral chain, and pass to the abdominal sympathetic and thence to the sciatic nerve. They are controlled by a centre in the upper lumbar region of the cord; those for the upper limbs leave the cord by the sixth, seventh, and eighth anterior thoracic roots, have cell stations in the ganglion stellatum, and ultimately pass to the ulnar and median nerves; they are controlled by a centre in the cervical enlargement of the cord. The secretory fibres for the head pass in the cervical sympathetic, and in some branches of the fifth cranial nerves. These subsidiary centres are dominated by one in the medulla oblongata (Adamkiewicz). These facts have been obtained by experiments on animals (cat, horse).

The sweat-centres may be excited directly by venous blood, as in asphyxia; or by over-heated blood (over 45° C.); or by certain drugs (see further); or reflexly by stimulation of afferent nerves such as the crural and peroneal.

Nervous diseases are often accompanied with disordered sweating; thus unilateral perspiration is seen in some cases of hemiplegia; degeneration of the anterior nerve-cells of the cord may cause stoppage of the secretion. It is sometimes increased in paralysed limbs.

The changes that occur in the secreting cells have been investigated by Renaut in the horse. When charged they are clear and swollen, the nucleus being situated near their attached ends;

when discharged they are smaller, granular, and their nucleus is more central.

The sweat, like the urine, must be regarded as an excretion, the secreting cells eliminating substances formed elsewhere.

Composition of the Sweat.—Sweat may be obtained in abundant quantities by placing the animal or man in a closed hot-air bath, or from a limb by enclosing it in a vessel made air-tight with an elastic bandage. Thus obtained, it is mixed with epidermal scales and a small quantity of fatty matter from the sebaceous glands. The continual shedding of epidermal scales is in reality an excretion. Keratin, of which they are chiefly composed, is rich in sulphur, and, consequently, this is one means by which sulphur is removed from the body.

The reaction of sweat is acid, and the acidity, as in the urine, is due to acid sodium phosphate. In profuse sweating, however, the secretion usually becomes alkaline or neutral. It has a peculiar and characteristic odour, which varies in different parts of the body, and is due to volatile fatty acids; its taste is saltish, its specific gravity about 1005.

In round numbers the percentage of solids is 1·2, of which 0·8 is inorganic matter. The following table is a compilation from several analyses:—

Water . .	98·88	per cent.	
Solids . .	1·12	,,	
Salts . .	0·57	,,	
NaCl . .	0·22 to 0·33	,,	
Other salts .	0·18	,,	(alkaline sulphates, phosphates, lactates, and potassium chloride)
Fats . .	0·41	,,	(including fatty acids and isocholesterin)
Epithelium .	0·17	,,	
Urea . .	0·08	,,	

The salts are in kind and relative quantity very like those of the urine. Funke was unable to find any urea, but most other observers agree on the presence of a minute quantity. It appears to become quickly transformed into ammonium carbonate. The proteid which is present is probably derived from the epithelial cells of the epidermis, sweat-glands, and sebaceous glands, which are suspended in the excretion; but in the horse there is albumin actually in solution in the sweat.

Abnormal, Unusual, or Pathological Conditions of the Sweat.—*Drugs.*—Certain drugs (sudorifics) favour sweating, *e.g.*, pilocarpine, Calabar bean, strychnine, picrotoxine, muscarine, nicotine, camphor, ammonia. Others diminish the secretion, *e.g.*, atropine and morphine in large doses.

Large quantities of water, by raising the blood-pressure, increase the perspiration.

Some substances introduced into the body reappear in the sweat, *e.g.*, benzoic, tartaric, and succinic acids readily, quinine and iodine with more difficulty. Compounds of arsenic and mercury behave similarly.

Diseases.—Cystin has been found in some cases of cystinuria; dextrose in diabetic patients; bile-pigment in those with jaundice (as evidenced by the staining of the clothes); indigo in a peculiar condition known as chromidrosis; blood or hæmatin derivatives in red sweat; albumin in the sweat of acute rheumatism, which is often very acid; urates and calcium oxalate in gout; lactic acid in puerperal fever, and occasionally in rickets and scrofula.

Kidney Diseases.—The relation of the secretion of the skin to that of the kidneys is a very close one. Thus copious secretions of urine, or watery evacuations from the alimentary canal, coincide with dryness of the skin; abundant perspiration and scanty urine generally go together. In the condition known as *uræmia* (see p. 556), when the kidneys secrete little or no urine, the percentage of urea rises in the sweat; the sputum and the saliva also contain urea under those circumstances. The clear indication for the physician in such cases is to stimulate the skin to action by hot-air baths and pilocarpine, and the alimentary canal by means of purgatives. In some of these cases the skin secretes urea so abundantly that when the sweat dries on the body, the patient is covered with a coating of urea crystals.

Varnishing the Skin.—By covering the skin of such an animal as a rabbit with an impermeable varnish, the temperature is reduced, a peculiar train of symptoms set up, and ultimately the animal dies. If, however, cooling is prevented by keeping such an animal in warm cotton-wool, it lives longer. Varnishing the human skin does not seem to be dangerous. Many explanations have been offered to explain the peculiar condition observed in animals; retention of the sweat would hardly do it; the blood is not found *post-mortem* to contain any abnormal substance, nor is it poisonous when transfused into another animal. Cutaneous respiration is so slight in mammals that stoppage of this function cannot be supposed to cause death. The animal, in fact, dies of cold; the normal function of the skin in regulating temperature is interfered with, and it is animals with delicate skins which are most readily affected.

CHAPTER XXXIX

GENERAL METABOLISM

THE word *metabolism* has been often employed in the preceding chapters, and, as there explained, it is used to express the sum total of the chemical exchanges that occur in living tissues. The chemical changes have been considered separately under the headings Alimentation, Excretion, Respiration, etc. We have now to put our knowledge together, and consider these subjects in their relation to one another.

The living body is always giving off by the lungs, kidneys, and skin the products of its combustion, and is thus always tending to lose weight. This loss is compensated for by the intake of food and of oxygen. For the material it loses, it receives in exchange fresh substances. If, as in a normal adult, the income is exactly equal to the expenditure, the body-weight remains constant. If, as in a growing child, the income exceeds the expenditure, the body gains weight; and if, as in febrile conditions, or during starvation, the expenditure exceeds the income, the body wastes.

The first act in the many steps which constitute nutrition is the taking of food, the next digestion of that food, the third absorption, and the fourth assimilation. In connection with these subjects, it is important to note the necessity for a mixed diet, and the relative and absolute quantities of the various proximate principles which are most advantageous. Assimilation is a subject which is exceedingly difficult to describe; it is the act of the living tissues in selecting, appropriating, and making part of themselves the substances brought to them by the nutrient blood-stream from the lungs on the one hand, and from the alimentary canal on the other. The chemical processes involved in some of these transactions have been already dwelt on in connection with the functions of the liver and other secreting organs, but even there our information on the subject is limited; much more is this the case in connection with other tissues. Assimilation, or the building up of the living tissues, may, to use Gaskell's expression, be spoken of as *anabolic.*

Supposing the body to remain in the condition produced by these anabolic processes, what is its composition? A glance through the chapters on the cell, the blood, the tissues, and the organs will convince the inquirer that different parts of the body have very different compositions; still, speaking of the body as a whole, Volkmann and Bischoff state that it contains 64 per cent. of water, 16 of proteids (including gelatin), 14 of fat, 5 of salt, and 1 of carbohydrates. The carbohydrates are thus the smallest constituent of the body; they are the glycogen of the liver and muscles, and small quantities of dextrose in various parts.

The most important, because the most abundant of the tissues of the body, is the muscular tissue. Muscle forms about 42 per cent. of the body-weight,* and contains, in round numbers, 75 per cent. of water and 21 per cent. of proteids; thus about half the proteid material and of the water of the body exist in its muscles.

The body, however, does not remain in this stable condition; even while nutrition is occurring, destructive changes are taking place simultaneously; each cell may be considered to be in a state of unstable equilibrium, undergoing *anabolic*, or constructive processes, on the one hand, and destructive, or *katabolic*, processes on the other. The katabolic series of phenomena commences with combustion; the union of oxygen with carbon to form carbonic acid, with hydrogen to form water, with nitrogen, carbon, and hydrogen to form urea, uric acid, creatinine, and other less important substances of the same nature. The formation of these last-mentioned substances, the nitrogenous metabolites, is, however, as previously pointed out, partly synthetical. The discharge of these products of destructive metabolism by the expired air, the urine, the sweat, and fæces is what constitutes excretion; excretion is the final act in the metabolic round, and the composition of the various excretions has already been considered.

An examination of the intake (food and oxygen) and of the output (excretion) of the body can be readily made; much more readily, it need hardly be said, than an examination of the intermediate steps in the process. A contrast between the two can be made by means of a balance-sheet. A familiar comparison may be drawn between the affairs of the animal body and those of a commercial company. At the end of the year the company presents a report in which its income and its expenditure are contrasted on two sides of a balance-sheet. This sheet is a summary of the monetary affairs of the undertaking; it gives few details, it gives none of the intermediate steps of the manner in which the property has been employed. This is given in the preliminary parts of the report, or may be entered into by still further examining the books of the company.

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* The following is in round numbers the percentage proportion of the different structural elements of the body: skeleton, 16; muscles, 42; fat, 18; viscera, 9; skin, 8; brain, 2; blood, 5.

In the parts of this book that precede this chapter I have endeavoured to give an account of various transactions that occur in the body. I now propose to present a balance-sheet. Those who wish still further to investigate the affairs of the body may do so by the careful study of works on physiology; still, text-books and monographs, however good, will teach one only a small amount; the rest is to be learnt by practical study and research; and we may compare physiologists to the accountants of a commercial enterprise, who examine into the details of its working. Sometimes, in business undertakings, a deficit or some other error is discovered, and it may be that the source of the mistake is only found after careful search. Under these conditions, the accountants should be compared to physicians, who discover that something is wrong in the working of the animal body; and their object should be to ascertain where, in the metabolic cycle, the mistake has occurred, and subsequently endeavour to rectify it.

The construction of balance-sheets for the human and animal body may be summed up in the German word *Stoffwechsel*, or "*exchange of material*." A large number of investigators have applied themselves to this task, and from the large mass of material published, it is only possible to select a few typical examples. The subject has been worked out specially by the Munich school, under the lead of Pettenkofer and Voit.

The necessary data for the construction of such tables are:—

(1) The weight of the animal before, during, and after the experiment.

(2) The quantity and composition of its food.

(3) The amount of oxygen absorbed during respiration.

(4) The quantity and composition of urine, fæces, sweat, and expired air.

(5) The amount of work done, and the amount of heat developed. (The subject of animal heat will be considered in the next chapter.)

Water is determined by subtracting the amount of water ingested as food from the quantity lost by bowels, urine, lungs, and skin. The difference is a measure of the katabolism of hydrogen.

Nitrogen.—The nitrogen is derived from proteids and albuminoids, and appears chiefly in the urine as urea and uric acid. Minute quantities are eliminated as similar compounds in sweat and fæces. From the amount of nitrogen so found, the amount of proteids which have undergone katabolism is calculated. Proteids contain, roughly, 16 per cent. of nitrogen; so 1 part of nitrogen is equivalent to 6·3 parts of proteid; or 1 gramme of nitrogen to 30 grammes of flesh.

Fat and carbohydrate.—Subtract the carbon in the metabolised proteid (proteid contains 54 per cent. of carbon) from the total carbon eliminated by lungs, skin, bowels, and kidneys, and the difference represents fat and carbohydrate that have undergone metabolism.

The Discharge of Carbon.

The influence of food on the rate of discharge of carbonic acid is immediate. The increase after each meal, which may amount to 20 per cent., reaches its maximum in about one or two hours. This effect is most marked when the diet consists largely of carbohydrates.

About 95 per cent. of the carbon discharged leaves the organism as carbonic acid. The total insensible loss (= carbonic acid + water given off − oxygen absorbed) amounts in man to about 25 grammes per hour. Of the total hourly discharge of carbonic acid, less than 0·5 per cent. is cutaneous. The hourly discharge of carbonic acid in a man at rest is about 32 grammes, the weight of oxygen absorbed being 25 to 28 grammes in the same time. The hourly discharge of watery vapour is about 20 grammes.

As a volume of carbonic acid (CO_2) contains the same weight of oxygen as an equal volume of oxygen (O_2), it is obvious that, if all the absorbed oxygen were discharged as carbonic acid, the "respiratory quotient" (by volume) $= \frac{CO_2 \text{ expired}}{O_2 \text{ absorbed}}$ would be equal to 1. This, however, is not the case, the volume of oxygen absorbed being in excess of the carbonic acid discharged. In animals fed exclusively on carbohydrates (this would only be possible for a short time) equality is approached. The excess of oxygen is greatest when the diet consists largely of fats.

On a mixed diet, comprising 100 grammes of proteid, 100 of fat, and 250 of carbohydrates, with a carbonic acid discharge of 770 grammes daily, and a daily assumption of 666 grammes of oxygen, 560 grammes of the oxygen are discharged in the carbonic acid, about 9 in urea, and 97 grammes in the form of water (of which 78 grammes are formed from the hydrogen of the fat); the respiratory quotient is then 0·84. In hibernation the respiratory quotient sinks lower than in any other known condition (often less than 0·5), for the animal then lives almost entirely on its own fat. The discharge of carbonic acid is increased by muscular work, and the respiratory quotient also rises. Diminution of the surrounding temperature causes increased discharge of carbonic acid. (These points are all discussed more fully in Chapter XXIV.)

The Discharge of Nitrogen.

In man the minimum daily allowance of nitrogen is 15 grammes, or 0·02 per cent. of the body-weight; in the carnivora about 0·1 per cent.; in the ox, as an instance of a herbivorous animal, 0·005 per cent. In certain races of mankind (*e.g.* coolies) the nitrogen requirement is less than in Europeans, and evidence has been recently accumulating to show that even Europeans can maintain equilibrium on diets much scantier than what is usually stated to be the minimum (see p. 460).

In an animal fed exclusively on flesh, the discharge of nitrogen at first increases *pari passu* with the absorption of proteid, the absorption of oxygen being proportionately increased at the same time. The animal, however, gains weight from increase of fat, the proteid being split into what is called a nitrogenous moiety, which is burnt off, and a non-nitrogenous moiety which is converted into fat.

The discharge of nitrogen is not immediately or markedly influenced by muscular work (see p. 555); the increased combustion that occurs in working as compared with resting muscles falls chiefly on their non-nitrogenous constituents.

Balance of Income and Discharge in Health.

In Chapter XXVIII. tables are given of adequate diets; these will in our balance-sheets represent the source of income; the other side of the balance-sheets, the expenditure, consists of the excretions.

EXCHANGE OF MATERIAL ON AN ADEQUATE DIET
(Ranke's table).*

Income.			Expenditure.		
Foods.	Nitrogen.	Carbon.	Excretions.	Nitrogen.	Carbon.
Proteid . 100 gr.	15·5 gr.	53·0 gr.	Urea . 31·5 gr. Uric acid 0·5 ,,	14·4	6·16
Fat . . 100 ,,	0·0 ,,	79·0 ,,	Fæces . . .	1·1	10·84
Carbohydrates . 250 ,,	0·0 ,,	93·0 ,,	Respiration (CO_2)	0·0	208·00
	15·5 ,,	225·0 ,,		15·5	225·00

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* The above table was constructed from data derived from the observations of Prof. Ranke on himself. Though made many years ago, Ranke's tables still serve as typical and standard examples of metabolic balance-sheets.

In man the discharge of nitrogen per kilo. of body-weight is 0·21 gramme, and of carbon 3·03 grammes, the quotient

$\frac{\mathrm{C}}{\mathrm{N}} = 14{\cdot}5$. In carnivorous animals, which, according to Bidder and Schmidt, use 1·4 N and 6·2 C per kilo. per diem, $\frac{\mathrm{C}}{\mathrm{N}} = 4{\cdot}4$. In the human being on a flesh diet $\frac{\mathrm{C}}{\mathrm{N}} = 5{\cdot}2$; the exchange thus approaches the condition of the carnivora. This is illustrated by the following balance-sheet (Ranke):—

Income.			Expenditure.		
	Nitrogen.	Carbon.		Nitrogen.	Carbon.
Food . . .	62·3 gr.	279·6	Discharged by excretion .	44·0	263·0
Disintegration of tissues . .	...	45·9	Retained in store .	18·3	62·5
	62·3 ,,	325·5		62·3	325·5

The details of the above experiment may be given as illustrating the method of working out a problem in exchange of material: 1832 grammes of meat used as food yielded 3·4 per cent. of nitrogen, *i.e.* 62·3 gr., and 12·5 per cent. of carbon, *i.e.* 229·3 gr.; 70 gr. of fat added to the food yielded 72 per cent. of carbon, *i.e.* 50·3 gr.: 229·3 + 50·3 = 279·6 = total carbon in food. During the same period 86·3 gr. of urea were discharged, containing 46·6 per cent., *i.e.* 40·4 gr. of nitrogen, and 20 per cent., *i.e.* 17·3 gr. of carbon, to which must be added 2 gr. of uric acid, containing 33 per cent., *i.e.* 0·66 gr. of nitrogen, and 35 per cent., *i.e.* 0·7 gr. of carbon. Further, 2·9 gr. of nitrogen and 14 gr. of carbon were discharged in the fæces, and 231 gr. of carbon as carbonic acid in the expired air. Hence the total discharge of nitrogen = 40·4 + 0·66 + 2·9 = 44 gr., and the total discharge of carbon = 17·3 + 0·7 + 14 + 231 = 263 gr. Deducting the quantity of nitrogen discharged from that taken in, 18·3 gr. must have been retained in the body, as 108 gr. of proteid, and consequently 53 per cent. of that weight = 62·5 gr. of carbon, were also retained. Comparing the quantity of carbon disposed of in the twenty-four hours with the quantity introduced as food, we find the former is in excess by 45·9 gr., which must have been derived from the disintegration of the fat of the body.

Another table of exchange of material on adequate diet may be quoted from the work of Pettenkofer and Voit. This takes into account the elimination of water as well as of carbon and nitrogen. In the first experiment the man did no work.

Income.			Expenditure.			
Food.	Nitrogen.	Carbon.	Excretions.	Nitrogen.	Carbon.	Water.
Proteid . 137 gr.	19·5	315·5	Urine .	17·4	12·7	1279
Fat . . 117 ,,			Fæces .	2·1	14·5	83
Carbohydrate . 352 ,,			Expired air .	...	248·6	828
Water . 2016 ,,	...	...				
				19·5	275·8	2190

Here the body was in nitrogenous equilibrium, and it eliminated more water than it took in by 174 grammes, this being derived from oxidation of hydrogen. It stored 39·7 grammes of carbon, which is equivalent to 52 grammes of fat.

The next table gives the results of an experiment on the same man on the same diet, but who did active muscular work during the day:—

Expenditure.	Nitrogen.	Carbon.	Water.
Urine	17·4	12·6	1194
Fæces	2·1	14·5	94
Expired air	...	309·2	1412
	19·5	336·3	2700

It is important to notice that the discharge of nitrogen was unaltered while that of both carbon and hydrogen was increased.

Inanition or Starvation.

The income from without is, under these circumstances, *nil;* expenditure still goes on, as a result of the disintegration of the tissues; the amount of disintegration is measured by the discharges in the manner already described. The following table from Ranke's experiment on himself represents the exchange for a period of twenty-four hours, twenty-four hours having elapsed since the last meal.

Disintegration of Tissue.			Expenditure.		
	Nitrogen.	Carbon.		Nitrogen.	Carbon.
Proteid . 50 gr.	7·8	26·5	Urea . 17 gr.	7·8	3·4
Fat . 199·6 ,,	0·0	157·5	Uric acid 0·2 ,,		
			Respiration (CO_2)	0·0	180·6
	7·8	184·0		7·8	184·0

The discharge of nitrogen per kilo. of body-weight was reduced to 0·1, $\frac{\mathrm{C}}{\mathrm{N}}$ being 23·5. In carnivorous animals, in prolonged inanition, the discharge of nitrogen per kilo. is 0·9 and $\frac{\mathrm{C}}{\mathrm{N}} = 6{\cdot}6$.

During starvation the man or animal gradually loses weight; the temperature, after a preliminary rise, sinks; the functions get weaker by degrees, and ultimately, when death ensues, the total weight lost varies from 0·3 to 0·5 of the original body-weight.

The age of the animal influences the time at which death occurs, old animals withstanding the effects of hunger better than young ones. This statement was originally made by Hippocrates, and was borne out by the experiments of Martigny and Chossat. Young animals lose weight more quickly, and die after a smaller loss of weight, than old ones.

The excretion of nitrogen falls quickly at the commencement of starvation; it reaches a minimum which remains constant for several days; it then rises when the fat of the animal has been used up, and then quickly falls with the onset of symptoms of approaching death.

The sulphates and phosphates in the urine show approximately the same series of changes.

The discharge of carbonic acid and the intake of oxygen fall, but not so quickly as the body loses weight; it is not until quite the last stages that these are small in proportion to one another.

The fæces become smaller and smaller in quantity until no discharge from the rectum occurs at all.

The amount of bile secreted also falls; but bile is found in the gall-bladder and intestine after death.

Taking the total loss of weight as 100, the loss due to that of individual organs may be stated as follows (Voit):—

Bone	5·4	Pancreas	0·1	Brain and cord	0·1
Muscle	42·2	Lungs	0·3	Skin and hair	8·8
Liver	4·8	Heart	0·0	Fat	26·2
Kidneys	0·6	Testes	0·1	Blood	3·7
Spleen	0·6	Intestines	2·0	Other parts	5·0

Some organs, such as heart and brain, thus lose but little weight; the loss of weight is greatest in the muscles, fat, skin, liver, and blood. Of the muscles, the great pectoral muscles waste most. Death may be delayed somewhat by artificial warmth, but ultimately occurs from asthenia, sometimes accompanied by convulsions.

Exchange of Material with various Diets.

The reasons why a mixed diet is necessary have been already explained (Chap. XXVIII.). Numerous experiments have, however, been made in the study of metabolism on abnormal diets.

Feeding with meat.—As the chief solid in meat is proteid, one must take either too much nitrogen or too little carbon. The principle that underlies Banting's method of treating obesity is to give meat almost exclusively: the individual then derives the additional supply of carbon necessary for combustion from his own adipose tissue. We have already seen that this may be and often is counteracted by the laying on of fat which comes from the non-nitrogenous moiety of the proteid.

Feeding with fat.—If an animal receives fat only, the nitrogenous excreta are derived from the disintegration of tissue without any corresponding supply of nitrogen being supplied in exchange in the food. When fat only is given, or a large excess of fat exists in the food, the respiratory quotient falls. F. Hofmann fed a dog on a mixture of a large amount of fat and a small amount of proteid. After death the quantity of fat found in the body was such that only a small part could have been derived from the proteid, the greater amount being directly derived from the fat of the food. The animal, moreover, lays on fat in which palmitin, stearin, and olein are mixed in a definite proportion; this proportion is often different in the fat of the food. In addition to this an animal will fatten (laying on fat with its usual composition) on fatty food, such as spermaceti, which contains no glycerides.

Feeding with carbohydrates.—The respiratory quotient approaches unity when carbohydrates alone are taken. So far as regards nitrogen the animal is in a state of inanition, as when fat alone is taken. If given in combination with other foods, both carbohydrates and fat act as proteid-sparing foods.

The following table is from Pettenkofer and Voit, and illustrates what happens in a dog on a mixed diet of flesh and carbohydrates.

Food.				Changes in the Body.			Fat.		
Flesh.	Starch.	Sugar.	Fat.	Amount of proteid decomposed calculated from urea excreted.	Proteid gained or lost by the body.	Amount of carbohydrates decomposed.	From fat of food.	Lost from the body.	Derived from food other than fat.
0	379	...	17	211	−211	379	+17	...	24
0	608	...	22	193	−193	608	+22	...	22
400	210	...	10	436	− 36	210	+10	− 8	...
400	...	227	...	393	+ 7	227	...	−25	...
400	344	...	6	413	− 13	344	+ 6	...	39
500	167	...	6	530	− 30	167	+ 6	...	8
500	...	182	...	537	− 37	182	...	...	16
800	379	...	14	608	+192	379	+14	...	55
1500	172	...	4	1475	+ 25	172	+ 4	...	43
1800	379	...	10	1469	+331	379	+10	...	112
2500	...	...	...	2512	+ 12	0	...	...	57

Even when the diet consists wholly of carbohydrates, fat is laid on; the fat laid on when meat and starch are both present in the food comes partly from the proteid and partly from the carbohydrate of the food. When no carbohydrate is given at all, as in the last experiment, the nitrogenous metabolism is raised. Carbohydrate food is thus when given with other foods both fat-sparing and proteid-sparing. The formation of fat from carbohydrates was first observed in pigs by Lawes and Gilbert, and has since been confirmed by numerous investigators.

One of the most important instances of the carbohydrate origin of fat is the formation of bees'-wax.

Instances of the formation of fat from proteids are (1) the laying on of fat in carnivorous animals; (2) the formation of adipocere, a wax-like material which forms in the muscles of corpses buried in damp soil, or allowed to remain in water; (3) the gradually increasing quantity of fat in old cheeses.

The most striking examples of the formation of fat by intracellular metabolic processes is seen in fatty degeneration, and in that special form of this degeneration that occurs in the formation of milk. The blood contains a mere trace of fat, so milk formation is no mere filtration process. The food may, as in the case of cows, contain little or no fat.

Feeding with gelatin.—A diet containing gelatin alone will not support life. This fact is somewhat remarkable when one considers the closely allied chemical nature of gelatin and proteids. When gelatin alone is given, the body wastes, and the urea excreted is diminished as in inanition. If an enormous amount of gelatin is given the urea increases. Gelatin, however, like carbohydrates and fats, appears to be a "proteid-sparing" food, and if given mixed with proteids seems to protect the proteids from oxidation. Gelatin can thus be substituted for a part of the proteid in the food.

Feeding with "peptones."—In the present day, when artificially digested foods are so much employed, it is of great importance that their nutritive value should be known. Here experimental and clinical evidence coincide in a most favourable way in relation to their nutritive value. Albumoses and the preparations called peptone in commerce, which are in reality mainly albumoses, have the same nutritive value as meat.

Concentrated or artificially digested foods of this kind (Witte's peptone, plasmon, somatose, etc.) must naturally be distinguished from beef-tea and extracts of meat of which there are so many in the market, but which are mere stimulants and are valueless for nutrition (see p. 469).

Effect of Varying External Conditions on Exchange of Material.

Effect of atmospheric temperature.—In warm-blooded animals the effect of a low surrounding temperature is to increase katabolism, or combustion in the body; the body loses more heat, and therefore more must be produced to keep the animal's temperature within normal limits. The effect of a rise of atmospheric temperature is the reverse. In cold-blooded animals, *i.e.*, animals whose temperature varies with that of the surrounding atmosphere, a rise or fall of the latter is accompanied respectively with a rise or fall of combustion in the body. Pembrey has shown that warm-blooded animals in an embryonic condition are practically cold-blooded; that is, their metabolism, body temperature, and the external temperature vary directly the one with the others.

Alterations of body temperature.—If the changes of the external temperature are so great as to cause a rise (as in steam-baths) or a fall (as in hibernation) of body temperature, the metabolic changes are increased and decreased respectively, as in cold-blooded animals.

Effect of removal of blood from the body.—The chief effect of a removal of blood from the body is the speedy formation of new blood-corpuscles. The intake of oxygen and discharge of carbonic acid are lessened, and the output of urea is increased. The menstrual flow and epistaxis in strong, healthy people cause no alteration in exchange of material.

Exchange of Material in Diseases.

Fever.—Fever is a condition in which the temperature of the body is raised above the normal, and the degree to which it is raised is a measure of the intensity of the febrile condition. A rise of temperature may be produced either by increased production of heat, due to the increase of katabolic processes in the body, or to a diminished loss of heat from the body. A mere increase in the production of heat does not necessarily produce fever. By administering an excess of food, combustion is increased in the body; but in the healthy individual this does not produce a rise of temperature, because *pari passu* with the increased production there is increased loss of heat. Similarly, diminution in the loss of heat, such as occurs on a hot as compared with a cold day, does not produce fever,* because the production of heat within the body is correspondingly diminished. In fever there is increased production of heat, as is seen by the study of exchange of material; the intake of food is, as a rule, very small; the discharge of nitrogen and carbon results from the disintegration of tissues, which, as compared with that in simple inanition, is large; the tissues are said to be in a labile condition, that is, they are easily broken down. In most febrile states, the skin is dry, the sweat-glands, like most of the secreting organs of the body, being comparatively inactive, and so the discharge of heat is lessened. The skin may, however, sometimes be bathed in perspiration, and yet high fever be present. The essential cause of the high temperature is neither increased formation nor diminished discharge of heat, but an interference with the reflex mechanism, which in health operates so as to equalise the two.

Increased nitrogenous metabolism in fever has been observed in pneumonia, in pyæmia, and in other febrile conditions. Ringer showed the correspondence in temperature and output of nitrogen very clearly in intermittent fever (ague).

What is known as the epicritical increase of urea is the greatly increased secretion of urea that occurs at the commencement of the defervescence of a fever. It is probably not due to an increased formation of urea, but to the removal of urea which has accumulated, owing to the fact that the kidneys have been acting sluggishly during the height of the fever.

Increased output of carbonic acid also occurs in fever.

Other changes noted in fever are a rapid loss of the liver glycogen, a lessening of chlorides in the urine, and often an increase of the urobilin in the urine.

The following table illustrates exchange of material in fever, no food being taken:—

Income.			Expenditure.		
Disintegration of tissue.	Nitrogen.	Carbon.	Excretions.	Nitrogen.	Carbon.
Proteid . 120 gr.	18·6	63·6	Urea and uric acid . 40 gr.	18·6	8·3
Fat . 205·7 ,,	0·0	157·4	Respiration (CO_2) . 780 ,,	0·0	212·7
	18·6	221·0		18·6	221·0

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* A febrile condition does occur on undue exposure to a tropical sun, for instance in soldiers in India; this is mainly due to their tight-fitting and otherwise unsuitable clothing, which interferes with the proper action of the skin.

Compare this table with that at the bottom of p. 589.

Diabetes mellitus.—In addition to the presence of sugar in the urine in this disease, the most marked symptoms are intense thirst and ravenous hunger. As a rule, diabetic patients digest their food well. The thirst is an indication of the necessity of replacing the large quantities of water lost by the kidneys; the hunger, that of replacing the great waste of tissues that occurs. For not only does the urine contain sugar, but, in addition, a great excess of urea and uric acid. The carbonic acid output is somewhat smaller than in health. In health the carbohydrates, after assimilation, give rise, by oxidation, to carbonic acid; in diabetes, all the carbohydrates do not undergo this change, but pass as sugar into the urine. Not that all the sugar of the urine is derived from carbohydrates, for many diabetics continue to pass large quantities when all carbohydrate food is withheld; under these circumstances, it must be derived from the destruction of proteid matter (see also pp. 516, 571). The increased production of organic acids which lessen the alkalinity of the blood should also be remembered (see pp. 518, 559).

Luxus Consumption.

In former portions of this book we have insisted on the fact that the food does not undergo combustion, or katabolic changes, until after it is assimilated, that is, until after it has become an integral part of the tissues. Formerly the blood was supposed to be the seat of oxidation; but the reasons why this view is not held now have been already given. When a student is first confronted with balance-sheets, representing metabolic exchanges, it is at first a little difficult for him to grasp the fact, that although the amount of nitrogen and carbon ingested is equal to the amount of the same elements which are eliminated, yet the eliminated carbon and hydrogen are not derived from the food direct, but from the tissues already formed; the food becomes assimilated and takes the place of the tissues thus disintegrated. Let us suppose we have a tube open at both ends and filled with a row of marbles; if an extra marble is pushed in at one end, a marble falls out at the other; if two marbles are introduced instead of one, there is an output of two at the other end; if a dozen, or any larger number be substituted, there is always a corresponding exit of the same number at the other end of the tube. This very rough illustration may perhaps assist in the comprehension of the metabolic exchanges.

The difficulty just alluded to, which a student feels, was also felt by the physiologists who first studied metabolism; and Voit formulated a theory, of which the following is the gist: All proteid taken into the alimentary canal appears to affect proteid metabolism in two ways: on the one hand, it excites rapid disintegration of proteids, giving rise to an immediate increase of urea; on the other hand, it serves to maintain the more regular proteid metabolism continually taking place in the body, and so contributes to the normal regular discharge of urea. It has been, therefore, supposed that the proteid which plays the first of these two parts is not really built up into the tissues, does not become living tissue, but undergoes the changes that give rise to urea, somewhere outside the actual living substance. The proteids are therefore divided into "tissue-proteids," which are actually built up into living substance, and "floating or circulating proteids," which are not thus built up, but by their metabolism outside the living substance set free energy in the form of heat only. It was at this time erroneously supposed that the exclusive use of proteid food was to supply proteid tissue elements, and that vital manifestations other than heat had their origin in proteid metabolism, the metabolism of fats and carbohydrates giving rise to heat only. Hence, when it was first surmised that a certain proportion of proteids underwent metabolism, which gave rise to heat only, this appeared to be a wasteful expenditure of precious material, and the metabolism of this portion of food was spoken of as a "luxus consumption," a wasteful consumption. There were many deductions from this general theory to explain particular points, of these two may be mentioned: (1) In inanition, the urea discharged for the first few days is much greater than it is subsequently: this was supposed to be due to the fact that in the first few days all the floating capital was consumed; (2) the effect of feeding with a mixture of gelatin and proteid was supposed to be due to the fact that gelatin was able to replace "floating proteid," but not "tissue proteid."

This theory of Voit's, ingenious and plausible at first sight, has met with but little general acceptance, because so many observed facts are incompatible with it.

Sir Michael Foster writes as follows: "The evidence we have tends to show that in muscle (taking it as an instance of a tissue) there exists a framework of what we may call more distinctly living substance, whose metabolism, though high in quality, does not give rise to massive discharges of energy, and that the interstices, so to speak, of this framework are occupied by various kinds of material related in different degrees to this framework, and therefore deserving to be spoken of as more or less living, the chief part of the energy set free coming directly from the metabolism of some or other of this material. Both framework and intercalated material undergo metabolism, and have in different degrees their anabolic and katabolic changes; both are concerned in the life of the organism, but one more directly than the other. We can, moreover, recognise no sharp break between the intercalated material and the lymph which bathes it; hence such phrases as 'tissue proteid' and 'floating proteid' are undesirable if they are understood to imply a sharp line of demarcation between the 'tissue' and the blood or lymph, though useful as indicating two different lines or degrees of metabolism."

Sir John Burdon-Sanderson writes as follows: "The production of urea and other nitrogenous metabolites is exclusively a function of 'living material'; and this process is carried on in the organism with an activity which is dependent on the activity of the living substance itself, and on the quantity of material supplied to it. No evidence at present exists in favour of a 'luxus consumption' of proteid."

Professor Hoppe-Seyler, after stating that he can make out no clear distinction between the two varieties of proteid from Voit's own writings, proceeds as follows: "Voit states that the circulating proteid is no other than that which is dissolved in the tissue juice, which is derived from the lymph-stream, and ultimately from the circulating blood. He (Voit) further says: 'As soon as the proteid of the blood-plasma leaves the blood-vessels, and circulates among the tissue elements themselves, it is then the proteid of the nutrient fluid or circulating proteid. It is no longer proteid of the blood-plasma, nor yet is it the proteid of the lymph-stream.' The place where Voit situates his circulating proteid is beyond the ken of the anatomist; it is in a mysterious space between tissue-elements, blood-vessels, and lymph-vessels; the chemist meets with equal difficulties, as there is apparently no chemical difference between tissue proteid and circulating proteid. I can, therefore, arrive at no other conclusion than that these terms are not only useless, but unscientific, and are the outcome of speculations in a region where there is as yet no positive knowledge. These criticisms on Voit's theories do not, however, by any means lessen the importance and high value of the immense amount of practical research carried on by Voit and his pupils"

I have placed Sir Michael Foster's view first because it takes into account certain facts which tend to show that there are degrees in metabolism. The most important of these is the formation of amino-acids in the intestine. It is an undoubted fact that by feeding an animal on leucine and other amino-acids, the urea is increased. This transformation of leucine into urea occurs in the liver. It can hardly be supposed that leucine becomes to any great extent an integral part of the living framework of the liver cells, but like other extractives, and like aromatic compounds absorbed from the alimentary canal, it becomes a part of what Foster terms the intercalated material. Here it undergoes the final change, and is ultimately and apparently very rapidly discharged in the urine. Sheridan Lea, discussing the probable *rôle* of the amino-acids in the animal economy, compares it to the part played by the salts of the food. Neither salts nor extractives simply pass into the urine without fulfilling a useful purpose on their way; but the exact and specific use of each, whether on the synthetic or analytic side of metabolic phenomena, must be the subject of renewed research. (Read again in this connection the last paragraph on p. 520, which describes certain recent researches that show that leucine and similar simple substances may be actually synthesised into protoplasm. If this is ultimately found to be correct, the opinions expressed in the first part of the present paragraph will need modification.)

CHAPTER XL

ANIMAL HEAT

AMONG the most important results of the chemical processes we sum up under the term metabolism, is the production of heat. Heat, like mechanical motion, is the result of the katabolic side of metabolic processes; the result, or accompaniment, that is to say, of the formation of carbonic acid, water, urea, and other excreted products.

As regards temperature, animals may be divided into two great classes:—

(1) Warm-blooded or *homoiothermal* animals, or those which have an almost constant temperature. This class includes mammals and birds.

(2) Cold-blooded or *poikilothermal* animals, or those whose temperature varies with that of the surrounding medium, being always, however, a degree, or a fraction of a degree, above that of the medium. This class includes reptiles, amphibians, fish, embryonic birds and mammals, and probably most invertebrates.

The temperature of a man in health varies but slightly, being between 36·5° and 37·5° C. (98° to 99° F.). Most mammals have approximately the same temperature: horse, donkey, ox, 37·5° to 38°; dog, cat, 38·5° to 39°; sheep, rabbit, 38° to 39·5°; mouse, 37·5°; rat, 37·9°. Birds have a higher temperature, about 42° C. The temperature varies a little in different parts of the body, that of the interior being greater than that of the surface; the blood coming from the liver where chemical changes are very active is warmer than that of the general circulation; the blood becomes rather cooler in its passage through the lungs.

The temperature also shows slight diurnal variations, reaching a maximum about 4 or 5 P.M. (37·5° C.) and a minimum about 3 A.M. (36·8° C.); that is, at a time when the functions of the body are least active. If, however, the habits of a man are altered, and he sleeps in the day, working during the night, the times of the maximum and minimum temperatures are also inverted. Inanition causes the temperature to fall, and just at the onset of death it may be below 30° C. Active muscular exercise raises the temperature temporarily by about 0·5° to 1° C. Diseases may cause the temperature to vary considerably, especially those which we term febrile (see p. 592).

Although certain mechanical actions, such as friction, due to movements of various kinds, may contribute a minute share in the production of heat in the body, yet we have no knowledge as to the actual amount thus generated. The great source of heat is, as already stated, chemical action, especially oxidation. Any given oxidation will always produce the same amount of heat. Thus, if we oxidise a gramme of carbon, a known amount of heat is produced, whether the element be free or in a chemical compound. The following figures show the approximate number of heat-units produced by the combustion of one gramme of the following substances. A heat-unit, or calorie, is the amount of heat necessary to raise the temperature of one gramme of water 1° C.:—

Hydrogen	34662	Fat	9400
Carbon	8100	Cane sugar	3950
Urea	2530	Starch	4160
Albumin	5600		

It is, however, most important to remember that the "physiological heat-value" of a food may be different from the "physical heat-value," *i.e.*, the amount of heat produced by combustion in the body may be different from that produced when the same amount of the same food is burnt in a calorimeter. This is the case with the proteids, because they do not undergo complete combustion in the body, for each gramme of proteid yields a third of a gramme of urea, which has a considerable heat-value of its own. Thus albumin, which, by complete combustion, yields 5600 heat-units, has a physiological heat-value = 5600 *minus* one-third of the heat-value of urea (2530) = 5600 − 846 = 4754. Rubner has recently shown that this figure must be reduced to nearly 4000, as some of the imperfectly burnt products of decomposition of proteids escape as uric acid, creatinine, etc., in the urine, and there is a small quantity of similar substances in the fæces. Any difference between the physical and physiological heat-values of fats and carbohydrates may be neglected, provided all the fat and carbohydrate in the food is absorbed.

Of the heat produced in the body, it is estimated by Helmholtz that about 7 per cent. is represented by external mechanical work, and that of the remainder about four-fifths are discharged by radiation, conduction, and evaporation from the skin, and the remaining fifth by the lungs and excreta. This is only an average estimate, subject to much variation, especially in the amount of work done.

The following table exhibits the relation between the production and discharge of energy in twenty-four hours in the human organism at rest, estimated in calories.* The table conveniently takes the form of a balance-sheet in which production and discharge of heat are compared; to keep the body-temperature normal these must be equal. The basis of the table in the left-hand (income) side is the same as Ranke's diet (see p. 587):—

Production of heat.		*Discharge of heat.*	
Metabolism of	Calories.		
Proteid (100 gr.) . 100 × 4000 =	400,000	Warming water in food, 2·6 kilos. × 25° C. =	65,000
Fat (100 gr.) . 100 × 9400 =	940,000	Warming air in respiration, 16 kilos. × 25° × 0·24 =	96,000
Carbohydrates (=250 gr. starch) 250 × 4160 =	1,040,000	Evaporation in lungs, 630 gr. × 582 =	366,660
		Radiation, evaporation, etc., at surface, *plus* the thermal equivalent of mechanical work done accounts for the remainder	1,852,340
	2,380,000		2,380,000

The figures under the heading Production are obtained by multiplying the weight of food by its physiological heat-value. The figures on the other side of the balance-sheet are obtained as follows: The water in the food is reckoned as weighing 2·6 kilos. This is supposed to be at the temperature of the air taken as 12° C.; it has to be raised to the temperature of the body, 37° C., that is, through 25° C. Hence the weight of water multiplied by 25 gives the number of calories expended in heating it. The weight of air is taken as weighing 16 kilos.; this also has to be raised 25° C., and so to be multiplied by 25; it has further to be multiplied by the relative heat of air (0·24). The 630 grammes of water evaporated in the lungs must be multiplied by the potential or latent heat of steam at 37° C. (582); the portion of heat lost by radiation, conduction, and evaporation from the skin constitutes about four-fifths of the whole, and is obtained by deducting the three previous amounts from the total. This table does not take into account the small quantities of heat lost with urine and fæces. We are further supposing that the man remains of constant weight, so that there is no storage or loss of material, and, therefore, of energy in the body. He is also supposed to be at rest, and therefore the amount of work done is only what is called internal work, *i.e.*, maintaining the circulation, respiration, etc.

It need hardly be remarked that the above is a mere illustrative experiment. Changes in the diet, in the atmospheric temperature, in the temperature of the food taken, in the activity of the sweat-glands, in the amount of moisture in the atmosphere, and in the amount of work done, would considerably alter the above figures.

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* The calorie we are taking is sometimes called the small calorie; by some the word *calorie* is used to denote the amount of heat necessary to raise one kilogramme of water 1° C.

Calorimetry.—Calorimeters employed in chemical operations are not suitable for experiments on living animals. An animal surrounded by ice or mercury, the melting and expansion of which respectively are measures of the amount of heat evolved, would be under such abnormal conditions that the results would be valueless. Lavoisier, however, used an ice calorimeter in his experiments on animals.

The apparatus often employed is the water calorimeter. This was first used by Crawford (1788). Dulong's instrument is shown in fig. 443. The animal is placed in a metal chamber, surrounded by a water-jacket. There are also tubes for the entrance and exit of the inspired and expired gases respectively. The heat given out by the animal warms the water in the jacket, and is measured by the rise of temperature observed in the water, of which the volume is also known. The air which passes out from the chamber goes through a long spiral tube, passing through the water-jacket, and thus the heat is abstracted from it and measured.

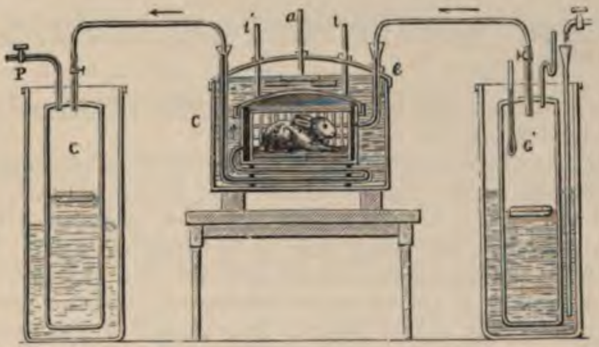

FIG. 443.—Dulong's Calorimeter: C, calorimeter, consisting of a vessel of cold water in which the chamber holding the animal is placed; G', gasometer from which air is expelled by a stream of water. The air enters the respiratory chamber. G, gasometer receiving the gases of expiration and the excess of air. *t*, *t'*, thermometers; *a*, a wheel for agitating the water. Observe the delivery-tube on the left is much twisted in the water-chamber, so as to give off its heat to the surrounding water. (From McKendrick's "Physiology.")

Air-Calorimeters are now, however, generally used. Fig. 444 is an outline sketch of the one which has been most used in this country.

It consists of two precisely similar chambers made of thin sheet copper. Each chamber has two walls between which is an air space; and the outer is covered by a thick casing of felt (F) to prevent fluctuations in the temperature of the surroundings from affecting the air in the air-space. The chambers are made perfectly air-tight, except for the ventilating tubes AA, A'A'. By means of these, the chambers are filled with perfectly dry air before the experiment is commenced. Leading from each air-space is a tube; the two tubes are connected to the two limbs of a manometer (M) shaped as in the figure, and containing oil of erigeron.

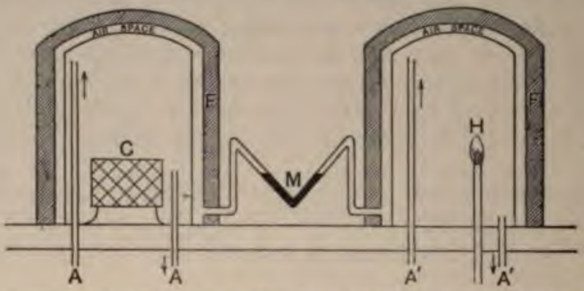

FIG. 444.—Air Calorimeter of Haldane, Hale White, and Washbourn. C, cage for animal. In order to make the conditions in both chambers as much alike as possible, an empty cage should be placed in the other chamber.

The action of the calorimeter is as follows:—In one chamber the animal, the heat production of which is to be ascertained, is placed within the cage C. In the other, hydrogen is burnt (H). Both chambers are shut, the tubes AA, A′A′ being clamped. The heat given off from the animal warms its chamber, and thus increases the pressure of the air in the air-space between the two copper walls of the chamber. This would lead to movement of the fluid in the manometer, but that the heat given off by the burning of the hydrogen increases at the same time the pressure in the air-space between the walls of its chamber. This latter increase of pressure tends to make the fluid in the manometer move in the other direction. If the fluid in the manometer remains stationary, the amount of heat given off by the animal is equal to that produced by the burning hydrogen; and during an experiment the fluid in the manometer is kept stationary by turning the hydrogen flame up and down. The amount of hydrogen burnt is estimated by the amount of water formed, and the heat of combustion of hydrogen being known, it is perfectly easy to calculate the calories produced, which equal those given off by the animal.

The applicability of the law of the conservation of energy to diverse chemical reactions has been amply demonstrated. In view of the chemical nature of metabolism, we might assume that the same law applies to the reactions taking place in the body, that it is in fact one of the fundamental laws of the universe. We have, however, no scientific right to assume in advance that no special laws are operative in living matter. The law therefore here requires experimental verification, and much labour has accordingly been devoted to this problem. The early work of Lavoisier, Crawford, Dulong, and others showed great discrepancies between the heat actually found and that calculated, but with the advance of knowledge and improvements of chemical methods and calorimetry, these have disappeared. It is to Rubner in particular that we owe the experimental demonstration of the law of the conservation of energy in the living organism.

The various tissues of the living body in the performance of their several functions break down and oxidise the proteids, fats, carbohydrates, and other materials of which they are composed, and seize upon the energy previously stored and thus liberated, converting it here into the invisible molecular motion of heat, there into the motion of visible masses of matter in the performance of work, and again into the energy of chemical change as the needs of the organism demand. Of these the liberation of heat is by far the greatest in amount, and for this reason, as well as to simplify calculations, it has become customary to express the available energy in terms of units of heat. The energy expended as work may be divided into (1) external work, *i.e.*, the work done on masses outside the body; and (2) internal work, *i.e.*, the physical and chemical changes produced within the body in the processes of breathing, digestion, circulation, and the like.

If the law of the conservation of energy applies to the animal organism, the following are its necessary consequences:—

1. If an animal is doing no external work, and is neither gaining nor losing substance, the potential energy of the food (expressed as its heat of combustion) will be equal to that of the excreta, *plus* that given off as heat, *plus* that of internal work.

2. If an animal is doing external work, and is neither gaining nor losing substance, the potential energy of the food will be equal to the potential energy of the excreta, *plus* that given off as heat, *plus* that of the internal work, *plus* that of the external work.

3. If an animal is doing no external work, but gaining or losing body substance, the potential energy of the food will equal the potential energy of the excreta, *plus* that given off as heat, *plus* that of the internal work, *plus* that of the gain by the body-substance (a loss by the body being regarded as a negative gain).

4. In an animal doing external work, and gaining or losing body-substance, the potential energy of the food will equal the potential energy of the excreta, *plus* that given off as heat, *plus* that of the internal and external work, *plus* that of the gain (positive or negative) of the body-substance.

In actual experimentation it is practically impossible to adjust the food so that there is no gain or loss of body-substance, hence experiments necessarily fall under (3) or (4); and the majority under (3).

The quantities to be determined, then, are:—

i. Potential energy of the food.

ii. Potential energy of excreta (fæces, urine, etc).

iii. The heat produced (including that into which any mechanical work is converted).

iv. The potential energy of the gain or loss of body-substance.

If, then, the equality stated under (3) and (4) is found to exist, we shall be justified in the conclusion that the law of the conservation of energy applies to the animal body. This is what the painstaking work of Rubner, Laulanié, Atwater, and others has succeeded in showing is actually the case.

Regulation of the Temperature of Warm-blooded Animals.

We have seen that heat is produced by combustion processes, and lost in various ways. In order to maintain a normal temperature, both sides of the balance-sheet must be equal. This equalisation may be produced by the production of heat adapting itself to variations in discharge, or by the discharge of heat adapting itself to variations in production, or lastly, and more probably, both sets of processes may adapt themselves mutually to one another. We have, therefore, to consider regulation (1) by variations in loss, and (2) by variations in production.

Regulation by Variations in Loss.—The two means of loss susceptible of any amount of variation are the lungs and the skin. The more air that passes in and out of the lungs, the greater will be the loss in warming the expired air and in evaporating the water of respiration. In such animals as the dog, which perspire but little, respiration is a most important means of regulating the temperature; and in these animals a close connection is observed between the production of heat and the respiratory activity. The panting of a dog when overheated is a familiar instance of this. A dog also, under the same circumstances, puts out its tongue, and loses heat from the evaporation that occurs from its surface. The great regulator, however, is undoubtedly the skin, and this has a double action. In the first place, it regulates the loss of heat by its vaso-motor mechanism; the more blood passing through the skin, the greater will be the loss of heat by conduction, radiation, and evaporation. Conversely, the loss of heat is diminished by anything that lessens the amount of blood in the skin, such as constriction of the cutaneous vessels, or dilatation of the splanchnic vascular area. In the second place, the special nerves of the sweat-glands are called into action. Familiar instances of the action of these two sets of nerves are the reddening of the skin and sweating that occurs after exercise, on a hot day, or in a hot-air or vapour bath, and the pallor of the skin and absence of sensible perspiration on the application of cold to the body.

Regulation by Variations in Production.—The rate of production of heat in a living body, as determined by calorimetry, depends on a variety of circumstances. It varies in different kinds of animals. The general rate of katabolism of a man is greater than that of a dog, and of a dog greater than that of a rabbit. Probably every species has a specific coefficient, and every individual a personal coefficient of heat production, which is the expression of the inborn qualities proper to the living substance of the species and individual. Another factor is the proportion of the bulk of the animal to its surface area, the struggle for existence raising the specific coefficient of the animals in which the ratio is high. Other important considerations are the relation of the intake of food to metabolic processes, and the amount of muscular work which is performed. These various influences are themselves regulated by the nervous system, and physiologists have long suspected that afferent impulses arising in the skin or elsewhere may, through the central nervous system, originate efferent impulses, the effect of which would be to increase or diminish the metabolism of the muscles and other organs, and by that means increase or diminish respectively the amount of heat there generated. That such a metabolic or thermogenic nervous mechanism does exist in warm-blooded animals is supported by the following experimental evidence:—

(1) Though in cold-blooded animals a rise or fall of the surrounding temperature causes respectively a rise and fall of their metabolic activity, in a warm-blooded animal the effect is just the reverse. Warmth from the exterior demands a diminished production of heat in the interior, and *vice versâ*. For exceptions, see p. 592.

(2) That this is due to a reflex nervous impulse is supported by the fact that a warm-blooded animal, when poisoned by curare, no longer manifests its normal behaviour to external heat and cold, but is affected in the same way as a cold-blooded animal. Section of the medulla produces the same effects, as the nerve-channels, by which the impulses travel, are severed. When curare is given, the reflex chain is broken at its muscular end, the poison exerting its influence on the end-plates, and causing a diminution of the chemical tonus of the muscles. The centre of this thermotaxic reflex mechanism must be situated somewhere above the spinal cord; according to some observers, in the optic thalamus.

(3) The reflex mechanism is well exemplified in *shivering;* here the muscles are thrown into involuntary contraction, and so produce more heat, as the result of the stimulation of the skin by cold.

(4) Various injuries caused by accident, or purposely produced by puncture, or cautery, or electrical stimulation of limited portions of the more central portions of the brain, may give rise to great increase of temperature, not accompanied by other marked symptoms.

We thus see that the nervous system is intimately associated with the regulation of the temperature of the body. There is at least one—there may be several centres associated in this action. The centres receive afferent impulses from without; they send out efferent impulses by at least three sets of nerves: (1) the vaso-motor nerves, (2) the secretory nerves of the sweat-glands, (3) trophic or nutritional nerves. The first two sets of nerves, the vaso-motor and the secretory, affect the regulation of temperature on the side of discharge; the third set on the side of production.

The foregoing account of heat regulation does not take into account what after all is, at any rate in man, a very important factor, namely, the voluntary and artificial means which he employs, such as various kinds of clothing suitable to the climate, heating of rooms, and voluntary muscular exercise.

CHAPTER XLI

THE CENTRAL NERVOUS SYSTEM

We already know sufficient from our preliminary study of nerve-centres to be aware that the central nervous system is divided into the two main parts called the brain and spinal cord.

Fig. 445 shows the general arrangement of the cerebro-spinal axis, and some anatomical details concerning the membranes that envelop the brain and cord may here conveniently be added.

Membranes of the Brain and Spinal Cord.—The Brain and Spinal Cord are enveloped in three membranes—(1) the Dura Mater, (2) the Arachnoid, (3) the Pia Mater.

(1) The *Dura Mater*, or external covering, is a tough membrane composed of bundles of connective tissue which cross at various angles, and in whose interstices branched connective-tissue corpuscles lie: it is lined by a thin elastic membrane, on the inner surface of which is a layer of endothelial cells.

(2) The *Arachnoid* is a much more delicate membrane, very similar in structure to the dura mater, and lined on its outer or free surface by an endothelial membrane.

(3) The *Pia Mater* of the cord consists of two layers between which numerous blood-vessels ramify. In that of the brain only the inner of the two layers is represented. Between the arachnoid and pia mater is a network of fibrous tissue trabeculæ sheathed with endothelial cells: these sub-arachnoid trabeculæ divide up the sub-arachnoid space into a number of irregular sinuses. There are some similar trabeculæ, but much fewer in number, traversing the sub-dural space, *i.e.*, the space between the dura mater and arachnoid.

Pacchionian bodies are growths from the sub-arachnoid network of connective-tissue trabeculæ which project through small holes in the inner layers of the dura mater into the venous sinuses of that membrane. The venous sinuses of the dura mater have been injected from the sub-arachnoidal space through the intermediation of these villous outgrowths.

In the chapters preceding this one we have seen how all-pervading nervous action is; in connection with circulation, respiration, secretion, peristalsis, etc., the way in which such functions are regulated by nervous activity has taken up a considerable amount of space. Some of the facts there described will be better understood, or be seen in a clearer light, if the student turns back to them and studies them once more after he has grasped what we are going to consider in the chapters that follow this on the physiology of the central nervous system.

It would also be advisable, before he begins this subject, that he should once more read Chap. XVII. on nerve-centres, in order to refresh his memory concerning the elementary and fundamental problems in relation to nervous activity in these regions.

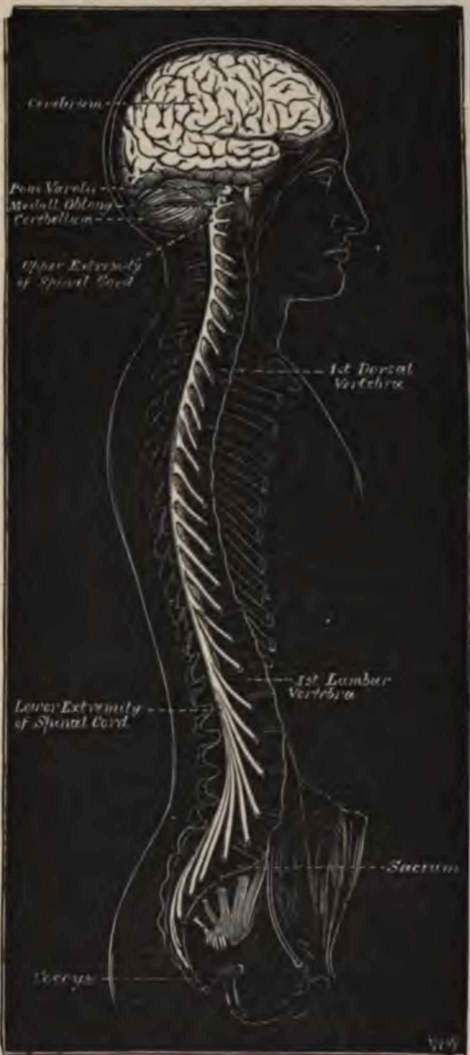

FIG. 445.—View of the cerebro-spinal axis of the nervous system. The right half of the cranium and trunk of the body has been removed by a vertical section; the membranes of the brain and spinal cord have also been removed, and the roots and first part of the fifth and ninth cranial, and of all the spinal nerves of the right side, have been dissected out and laid separately on the wall of the skull and on the several vertebræ opposite to the place of their natural exit from the cranio-spinal cavity. (After Bourgery.)

CHAPTER XLII

STRUCTURE OF THE SPINAL CORD

THE spinal cord is a column of nerve-substance connected above with the brain through the medium of the bulb, and situated in the spinal canal. In transverse section it is approximately circular, but the cord is not of the same size throughout its course. It exhibits two enlargements, one in the cervical, the other in the lumbar region. These are the situations whence the large nerves for the supply of the limbs issue. The cord terminates below, about the lower border of the first lumbar vertebra, in a slender filament of grey substance, the *filum terminale,* which lies in the midst of the roots of many nerves forming the *cauda equina.*

It is composed of grey and white matter; the white matter is situated externally, and constitutes its chief portion; the grey matter is in the interior, and is so arranged that in a transverse section of the cord it appears like two crescentic masses (the horns of each of which are called respectively the anterior and posterior cornua) connected together by a narrower portion or isthmus, called the posterior commissure (fig. 446). Passing through the centre of this isthmus in a longitudinal direction is a minute canal; in a transverse section it appears as a hole; this *central canal* of the spinal cord is continued throughout its entire length, and opens above into the space at the back of the medulla oblongata and pons Varolii, called the fourth ventricle. It is lined by a layer of columnar ciliated epithelium, and contains a fluid called *cerebro-spinal fluid.*

The spinal cord consists of two symmetrical halves, separated anteriorly and posteriorly by vertical *fissures* (the posterior fissure being deeper, but less wide and distinct than the anterior), and united in the middle by nervous matter which is usually described as forming two commissures—an *anterior* commissure in front of the central canal, consisting of medullated nerve-fibres, and a *posterior* commissure behind the central canal, consisting also of medullated nerve-fibres, but with more neuroglia, which gives the grey aspect to this commissure (fig. 446, B). Each half of the spinal cord is marked on the sides (obscurely at the lower part, but distinctly above) by

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ion, with the roots of the
hown ; the anterior nerve-
in c, the upper surface is
anterior median fissure;
he anterior nerve-roots are
ots are seen to sink; 5,
6, the posterior roots, the
; 7', the posterior primary
rt from the posterior root.

ortions, columns, or tracts, an *anterior*, *lateral*, and *posterior*. From the groove between the anterior and lateral columns spring the *anterior roots* of the spinal nerves (fig. 446, B and C, 5); and just in front of the groove between the lateral and posterior column the *posterior roots* enter (B, 6): a pair of roots on each side corresponds to each vertebra.

White matter.—The white matter of the cord is made up of medullated nerve-fibres, of different sizes, arranged longitudinally, and of a supporting material of two kinds, viz.:—(*a*) ordinary fibrous connective-tissue with elastic fibres, which is connected with septa from the pia mater which pass into the cord to carry the blood-vessels. (*b*) Neuroglia; the processes of the neuroglia-cells are arranged so as to support the nerve-fibres which are without the usual neurilemmal nerve-sheaths.

The general rule respecting the size of different parts of the cord is, that each part is in direct proportion to the size and number of nerve-roots given off from it. Thus the cord is very large in the middle and lower part of its cervical portion, whence arise the large nerve-roots for the formation of the brachial plexuses and the supply of the upper extremities; it again enlarges at the lowest part of its dorsal portion and the upper part of its lumbar, at the origins of the large nerves which, after forming the lumbar and sacral plexuses, are distributed to the lower extremities. The chief cause of the greater size at these parts of the spinal cord is increase in the quantity of grey matter; the white part of the cord (especially the lateral columns) becomes gradually and progressively smaller from above downwards, because a certain number of fibres coming down from the brain pass into the spinal grey matter at different levels.

Grey matter.—The grey matter of the cord consists of nerve-fibres, most of which are very fine and delicate, of nerve-cells with branching processes, and of an extremely delicate network of the primitive fibrillæ of axis-cylinders and of dendrites. This fine plexus is called *Gerlach's network*, and is mingled with the meshes of neuroglia. The neuroglia of the grey matter resembles that of the white, but instead of everywhere forming a close network to support the nerve-fibres, here and there it is in the form of a more open sponge-work to support the nerve-cells. It is especially developed around the central canal, which is lined with columnar ciliated epithelium, the cells of which at their outer end terminate in fine processes, which join the neuroglia network surrounding the canal, and form the *substantia gelatinosa centralis.* It is also developed at the tip of the posterior cornu of grey matter, forming what is known as the *substantia gelatinosa lateralis* of Rolando, which is much enlarged in the upper cervical region.

Groups of cells in the grey matter.—The multipolar cells of the grey matter are either scattered singly or arranged in definite groups.

(1) *Anterior horn cells.*—In the cervical and lumbar enlargements there are several groups of large multipolar cells in the anterior horn; in the thoracic region these are reduced to two, a mesial and a lateral group. The larger groups correspond with segments of the limbs, and in the cervical cord there is one special group from which the phrenic nerve arises for the supply of the diaphragm. The axons pass out by the anterior nerve-roots of the same side, but a few axons pass to the antero-lateral column of the same side, and by the white commissure to that of the opposite side. In birds, a few axons are stated to pass to the posterior roots.

(2) *Posterior vesicular column of Lockhart Clarke; generally known as Clarke's column.*—This is a group of large nerve-cells with their long

axis vertical. It lies at the base of the posterior horn, and is best marked in the thoracic region. Their axons pass into the direct cerebellar tract.

(3) *Intermedio-lateral group.*—This is seen in the outer part of the grey matter of the lateral horn, and is most distinct in the upper thoracic and lower cervical regions.

(4) *The middle cell column* lies in the middle of the crescent.

(5) The cells of the posterior horn are usually small; they are numerous, but are not disposed in special groups.

Columns and tracts in the white matter of the spinal cord.—The columns of the white matter which are marked out by the points from which the nerve-roots issue, are called the *anterior*, the *lateral*, and the *posterior* columns; the posterior is further divided by a septum of the pia mater into two almost equal parts, constituting the *postero-external* column, or *column of Burdach*, and the *postero-median*, or *column of Goll* (fig. 449). In addition to these columns, however, it has been shown that the white matter can be still further subdivided. These tracts in the white matter perform different functions in the conduction of impulses.

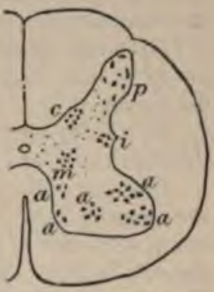

FIG. 447.—Section of half the spinal cord to show the principal groups of cells in the grey matter; *a*, groups of cells in the anterior horn; *c*, Clarke's column; *i*, intermedio-lateral group; *m*, middle cell column; *p*, scattered cells of the posterior horn. (Diagrammatic after Schäfer.)

The methods of observation are the following:—

(*a*) The *embryological* method. It has been found by examining the spinal cord at different stages of its development that certain groups of the nerve-fibres put on their myelin sheath at earlier periods than others, and that the different groups of fibres can therefore be traced in various directions. This is also known as the method of Flechsig.

(*b*) *Wallerian or degeneration method.*—This method depends upon the fact that if a nerve-fibre is separated from its nerve-cell, it wastes or degenerates. It consists in tracing the course of tracts of degenerated fibres, which result from an injury to any part of the central nervous system. When fibres degenerate below a lesion, the tract is said to be of *descending degeneration*, and when the fibres degenerate in the opposite direction, the tract is one of *ascending degeneration*. By the modern methods employed in staining the central nervous system, it has proved comparatively easy to distinguish degenerated parts in sections of the cord and of other portions of the central nervous system. Degenerated fibres have a different staining reaction when the sections are stained by what are called Weigert's and Pal's methods; this consists in subjecting them to a special solution of hæmatoxylin, and then to certain differentiating solutions. The degenerated fibres appear light yellow, whereas the healthy fibres are a deep blue. Marchi's method is even better. After hardening in Müller's fluid, Marchi's solution (a mixture of Müller's fluid and osmic acid) stains degenerated fibres black, and leaves the rest of the tissue unstained. Accidents to the central nervous system in man have given us much information upon this subject, but this has of late years been supplemented and largely extended by experiments on animals, particularly upon monkeys; and considerable light has been shed upon the conduction of impulses to and from the nervous system by the study of the results of section of different parts of the central nervous system, and of the spinal nerve-roots.

By these methods the tracts in the white matter have now been mapped out, and the principal ones are shown in the succeeding diagrams.

It will be convenient to begin by considering the result of cutting through the roots of the spinal nerves.

Cutting the anterior roots produces chromatolysis of the cells of the anterior horn from which they originate; this slow atrophy is the result of disuse of the axons which are cut and still remain attached to the cell-bodies. Wallerian degeneration is limited to the motor nerve-fibres on the distal side of the point of section. The fact that chromatolysis (see p. 202) occurs when the axon of a nerve-cell is cut through, furnishes us with a valuable method as ascertaining what nerve-cells various tracts originate from.

Cutting the posterior roots between the spinal ganglia and the cord leaves the peripheral part of the nerve healthy, and degeneration occurs in the portion of the root which runs into the cord, because the fibres are cut off from the cells of the spinal ganglion from which they grew. These degenerated nerve-fibres may be traced up the cord for a considerable distance. Each posterior root-fibre when it enters the cord bifurcates, the main branch passing upwards, and the shorter branch downwards, so that the degeneration is seen in a small tract called the comma tract (fig. 450) immediately below the point of entrance of the cut posterior root. The upgoing fibre is contained in the posterior column of white matter, and it terminates in the grey matter either in the cord itself at a higher level, or in the medulla oblongata.

Fig. 448 represents in a schematic way the manner in which the fibres of the two roots of a spinal nerve are connected to the grey matter in the cord.

1, 2, 3, 4 represent four cells of the anterior horn. Each gives rise to an axis-cylinder, process A, one of which is shown terminating in its final ramification in the end-plate of a muscular fibre M. Each of these four cells is further surrounded by an arborisation (synapse) derived from the fibres of the pyramidal tract P, which comes down from the brain.

According to Schäfer's recent work, the pyramidal fibres really terminate around the cells at the base of the posterior horn; these cells therefore act as intermediate cell-stations on the way to those in the anterior horn. This is not shown in the diagram.

A fibre of the posterior root is also shown; this originates from the cell G of the spinal ganglion; the process of this cell bifurcates,

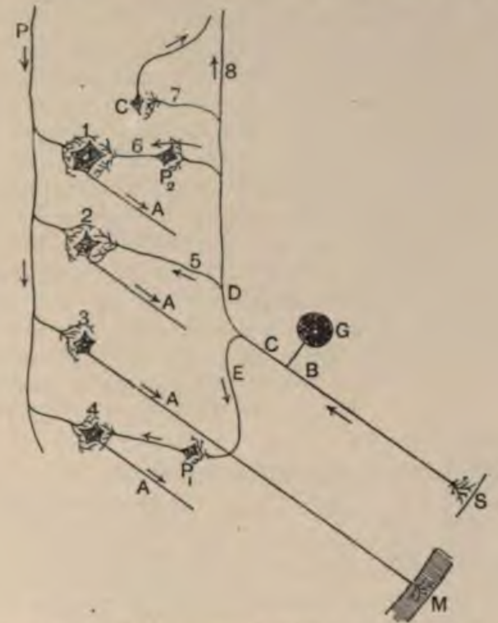

FIG. 448.—Course of nerve-fibres in spinal cord. (After Schäfer.)

one branch (B) passing to the periphery, where it ends in an arborescence in the skin (S); the arrow by the side of this branch represents the direction of conduction of the sensory impulses from the skin. An arrow in the opposite direction would indicate the direction of its growth. The other branch C passes into the spinal cord, where it again bifurcates; the branch E, a short one, passes downwards and ends in an arborisation around one of the small cells P_1 of the posterior cornu; from which a new axis-cylinder arises, and terminates around one of the multipolar cells (4) of the anterior horn.

The main division D travels up in the posterior column of the cord, and ends in grey matter at various levels. Some collaterals (5) terminate by arborising directly around the anterior cornual cells, principally of the same side; others (6) do so with an intermediate cell station in a posterior cornual cell P_2; others (7) arborise around the cells of Clarke's column (C) in the thoracic region of the cord, and from these cells fresh axis-cylinders carry up the impulse to the cerebellum in what is called the direct cerebellar tract, while the main fibre (8) may terminate in any of these ways at a higher level in the cord, or above the cord in the medulla oblongata. When we become acquainted with the structure of the medulla oblongata, we shall be able to trace these fibres further.

In general terms the anterior root-fibres pass out of the grey matter of the anterior horns, and after a short course leave the spinal cord in the anterior spinal nerve-roots. The posterior roots, on the other hand, do not pass to any great extent into the grey matter immediately, but into the white matter on the inner side of the posterior horn; in other words, they go into the column of Burdach (fig. 449); they pass up in this column, but gradually approach the middle line, and are continued upwards to the medulla in the column of Goll; but as they go up they become less numerous, as some terminate in the grey matter of the cord on the way in the manner described. A few fibres of the posterior root, however, travel for a short distance in a small tract on the outer side of the posterior horn; this is called the tract of Lissauer (fig. 451); the comma tract (fig. 450) has been already explained.

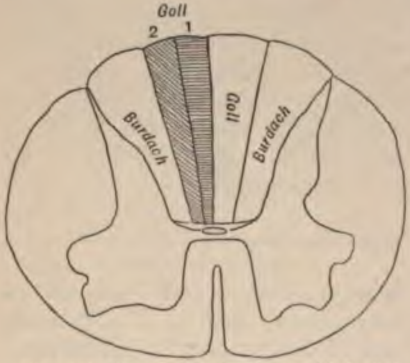

FIG. 449.—Degeneration in column of Goll after section of posterior nerve-roots.

Suppose now one cuts through several posterior roots between the spinal ganglia and the cord, so that the course of degeneration may be more readily traced. Immediately below the points of entrance of these nerve-roots, the comma tract will be found degenerated; immediately above, the degenerated fibres will be found in the column of Burdach; higher up in the cord they will be less numerous, and have approached the middle line; the fibres which enter the cord lowest get ultimately nearest the middle line, so that the greater part of the column of Goll is made up of sensory fibres from the legs; the fibres which enter the cord last, for instance those from the upper limbs and neck, pursue their course in the inner part of the column of Burdach.

The preceding figure (fig. 449) shows the degeneration in a section of the spinal cord, after the division of a number of nerve-roots on one side. The microscopic section is taken high up, so that all the degenerated fibres have passed into the column of Goll on the same side; the inner set (1) are shaded differently from the outer set (2), indicating that those nearest the middle line come from the lowest nerve-roots.

We may pass from this to consider the tracts of degeneration that occur when the spinal cord is cut right across in the thoracic region. Some tracts will be found degenerated in the piece of cord below the lesion; these consist of nerve-fibres that are connected with the nerve-cells in the brain; the principal ones are the pyramidal tracts. Other tracts are found degenerated in the piece of cord above the lesion; these consist of nerve-fibres that are connected with the nerve-cells of the spinal ganglia, or with the cells of the spinal cord itself below the lesion and are passing upwards.

In general terms we may say that the tracts which degenerate downwards are the motor tracts, and those which degenerate upwards are the afferent or sensory channels. We must also take into account groups of association fibres which unite together different regions of the cord; these are generally short tracts in which, therefore, degeneration can only be traced a short distance up or down. The long tracts are those which connect cord or spinal nerves with brain, like those of Goll and Burdach just mentioned, or the pyramidal tracts the main efferent pathways.

Tracts of Descending Degeneration (fig. 450).

(1.) *The crossed pyramidal tract.*—This is situated in the lateral column on the outer side of the posterior cornu of grey matter. At the lower part of the spinal cord it extends to the margin, but higher up it becomes displaced from this position by the interpolation of another tract of fibres, to be presently described, viz., the direct cerebellar tract. The crossed pyramidal tract is large, and may touch the grey matter at the tip of the posterior cornu, but is separated from it elsewhere. Its shape on cross section is somewhat like a lens, but varies in different regions of the cord, and diminishes in size from the cervical region downwards, its fibres passing off as they descend, to arborise around the nerve-cells and their branchings in the grey matter of the cord. The fibres of which this tract is composed are moderately large, but are mixed with some that are smaller.

(2.) *The direct or uncrossed pyramidal tract, or column of Türck.*—This tract is situated in the anterior column by the side of the anterior fissure. It ends in the mid or lower thoracic region of the cord.

The two pyramidal tracts come down from the brain; in the medulla oblongata, the greater number of the pyramidal fibres cross over to the other side of the cord which they descend; hence the term crossed pyramidal tract; a smaller collection of the pyramidal fibres goes straight on, on the same side of the cord, and these cross at different levels in the anterior commissure of the cord lower down; hence the disappearance of the direct pyramidal tract in the lower part of the cord. The fact that the crossed pyramidal tract of one side is the fellow of the direct pyramidal tract of the other side, is indicated in the diagram by the direction of shading (see fig. 450).

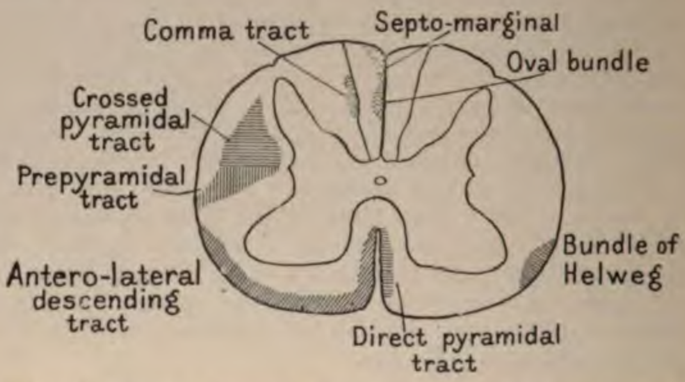

FIG. 450.—Tracts of descending degeneration. For the sake of clearness each is shown on only one side. (After Schäfer).

Mingled with the fibres of the crossed pyramidal tract are a few fibres of the pyramid which have not crossed in the medulla oblongata, and are therefore derived from the same side of the cerebrum (*uncrossed lateral pyramidal fibres*).

The pyramidal fibres are not found at all in vertebrates below the mammals. In the lower mammals they are very small, and in some rodents (rat, mouse, guinea-pig) they are placed in the posterior columns. The direct pyramidal tract is found only in man and the higher apes.

The paralysis that results from the section of the pyramidal tracts passes off very soon in many animals, whereas that which results from section of the anterior column and the adjacent part of the lateral column is more permanent. It is probable that the two tracts next to be described may be the second path for volitional impulses, and perhaps derive their importance from the fact that the impulses which travel down them are necessary in the maintenance of the tone of the anterior horn cells.

(3.) *Antero-lateral descending tract, or tract of Loewenthal,* lies by the side of the anterior median fissure, and extends along the margin of the cord towards the lateral column. These originate from the posterior longitudinal bundle of the medulla oblongata, and from other sources to be described later. They end by synapses in the anterior horn.

(4.) *The prepyramidal tract* (Monakow's bundle).—This is situated just in front of the crossed pyramidal tract. Its origin is in the cells of the red nucleus in the mid-brain. Its fibres end by arborisations in the grey matter about the middle of the crescent.

(5.) *Bundle of Helweg.*—The exact origin and destination of these fibres are not known: they can be traced from the neighbourhood of the olivary body in the medulla oblongata, and pass down in the anterior part of the lateral column in the cervical region.

(6.) *Short tracts in the posterior column.*—These are (*a*) the *Comma* tract; though this degenerates downwards, it is in reality a sensory tract, being composed, as we have already seen, of the branches of the entering posterior root-fibres which pass downwards on entering the cord. It is only found for a comparatively short distance below the actual lesion. (*b*) *Septo-marginal fibres;* these are few in number, and are mainly found near the median fissure, where they constitute the *oval bundle,* and near the posterior surface, where they form the *median triangle bundle.* These are doubtless short association tracts, and are mixed with others, especially in the ventral part of the posterior column, which have an "ascending" course.

Tracts of Ascending Degeneration (fig. 451).

(1.) *Postero-medial column, or column of Goll.*—This consists of fibres derived from the posterior roots of the sacral, lumbar, and lower thoracic nerves. These fibres enter the postero-lateral column, and gradually pass towards the mid-line, as already explained. They

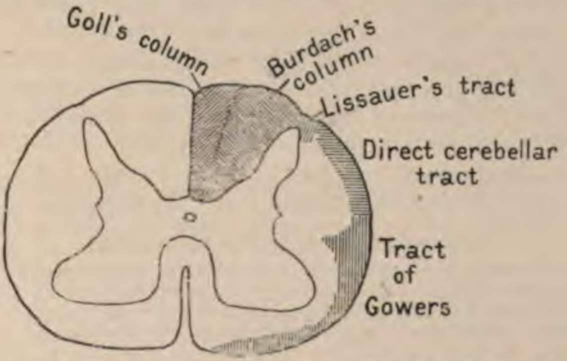

FIG. 451.—Tracts of ascending degeneration, shown on one side of the cord only. (After Schäfer).

end in the grey matter of the nucleus gracilis of the medulla oblongata.

(2.) *Postero-lateral column, or column of Burdach.*—Many of the fibres of this tract, which is also composed of the entering posterior nerve-roots, pass into the grey matter of the cord either immediately on entrance, or in their course upwards. The rest continue upwards to the medulla oblongata, but those from the lower roots pass into the column of Goll, as just stated; those from the upper roots continue to travel upwards in the column of Burdach, and end in the grey matter of the nucleus cuneatus in the medulla oblongata.

(3.) *Dorsal or direct cerebellar tract, or tract of Flechsig.*—This is found in the cervical and thoracic regions of the cord, and is situated between the crossed pyramidal tract and the margin. It degenerates on injury or section of the cord itself, but not on section of the posterior nerve-roots. In other words, its fibres are endogenous, *i.e.*, arise from cells within the grey matter of the cord; these cells are those of Clarke's column of the same side; the fibres are large ones.

(4.) *Ventral cerebellar or antero-lateral ascending tract, or tract of Gowers.*—This is situated in front of the crossed pyramidal and direct cerebellar tracts in the lumbar region, while in the thoracic and cervical regions it forms a narrow band at the margin of the cord, curving round even into the anterior column. Its fibres intermingle with those of the antero-lateral descending tract.

Both of these tracts, as their names indicate, go to the cerebellum; the dorsal cerebellar enters the cerebellum by its lower peduncle, while the ventral cerebellar enters by its superior peduncle. The fibres terminate by arborising around the cells of that part of the cerebellum known as the *vermis* or middle lobe. V. Gehuchten states that the ventral tract gives off a few fibres that enter the opposite cerebellar hemisphere by its middle peduncle.

(5.) *Tract of Lissauer, or posterior marginal zone.*—This is a small tract of ascending fibres situated at the outer side of the tip of the posterior horn. These are fine fibres from the posterior roots; they subsequently pass into the posterior column.

(6.) A number of association tracts have been differentiated by Flechsig's and Sherrington's method (see next paragraph).

Association fibres in the Spinal Cord.

The numerous short tracts already mentioned as demonstrable in the spinal cord are doubtless bundles of association fibres which connect its different levels together. The main difficulty of investigating them by the degeneration method has arisen from the fact that they are largely intermingled with, and so are hard to distinguish from the long tracts which connect brain and cord together. In 1853 Pflüger stated that reflex irradiation within the spinal cord always took place in an upward direction, but Sherrington in his work found many exceptions to this rule, and he sought for the paths which are capable of carrying the impulses down the cord by a very ingenious method. The spinal cord of a dog was completely divided across, and the animal was kept alive for a considerable time afterwards;

sufficient time was allowed to elapse (roughly about a year) for all traces of the degeneration due to this lesion to have disappeared. The cord is then left, as it were, like a cleaned slate, on which once more a new degeneration can be written without fear of confusion with a previous one. The second degeneration produced by such an operation as hemisection would then affect the intra-spinal fibres only, all the long tracts from brain to cord having been wiped out by the first operation. The complete topography of all these fibres, which are very numerous, has not yet been worked out. The degenerated fibres are scattered throughout the white matter, but are most numerous at the margins of the cord. This is especially true for the longer fibres, and some of them appear to be very long indeed. In the case of the longer fibres there is no evidence of decussation; in the case of the shorter fibres there is some but not very conclusive evidence that they in part cross to the other side.

Complete transverse section of the spinal cord leads to:—

1. Loss of motion of the parts supplied by the nerves below the section on both sides of the body. The paralysis is not confined to the voluntary muscles, but includes the muscular fibres of the blood-vessels and viscera. Hence there is fall of blood-pressure, paralysis of sphincters, etc.
2. Loss of sensation in the same regions.
3. Degeneration, ascending and descending, on both sides of the cord.

Hemisection.—If the operation performed is not a complete cutting of the spinal cord across transversely, but a cutting of half the cord across, it is termed hemisection, or semi-section.

This operation leads to:—

1. Loss of motion of the parts supplied by the nerves below the section on the same side of the body as the injury.
2. Loss of sensation in the same region. The loss of sensation is not a very prominent symptom, and is limited to the sense of localisation and the muscular sense. The animal can still feel sensations of pain and of heat and cold.
3. Degeneration, ascending and descending, nearly entirely confined to the same side of the cord as the injury. The most important of these are shown in the photo-micrographs (fig. 452) on the opposite page, the small text beneath which should be carefully studied.

Differences in different regions of the spinal cord.—The outline of the grey matter and the relative proportion of the white matter varies in different regions of the spinal cord, and it is, therefore, possible to tell approximately from what region any given transverse section of the spinal cord has been taken. The white matter increases in amount from below upwards. The amount of grey matter varies; it is greatest in the cervical and lumbar enlargements, viz., at and about the 5th lumbar and 6th cervical nerve, and least in the thoracic region. The greatest development of grey matter corresponds with greatest number of nerve-fibres passing from the cord.

In the cervical enlargement the grey matter occupies a large proportion of the section, the grey commissure is short and thick, the anterior horn is blunt, whilst the posterior is somewhat tapering. The anterior and posterior roots run some distance through the white matter before they reach the periphery. At the extreme upper part of the cervical region, the end of the posterior horn is swollen out by excess of neuroglia into a rounded mass called the *substantia gelatinosa of Rolando.* The cervical cord is wider from side to side than from before back; this is owing to the great width of the lateral columns.

In the dorsal region the grey matter bears only a small proportion to the white, and the posterior roots in particular run a long course through the white matter after they enter the cord; the grey commissure is thinner and narrower than in the cervical region. The intermedio-lateral tract is here most marked, and forms a prominence often called the lateral horn. This is shown in fig. 452 C. Clarke's column is also confined to this region of the cord.

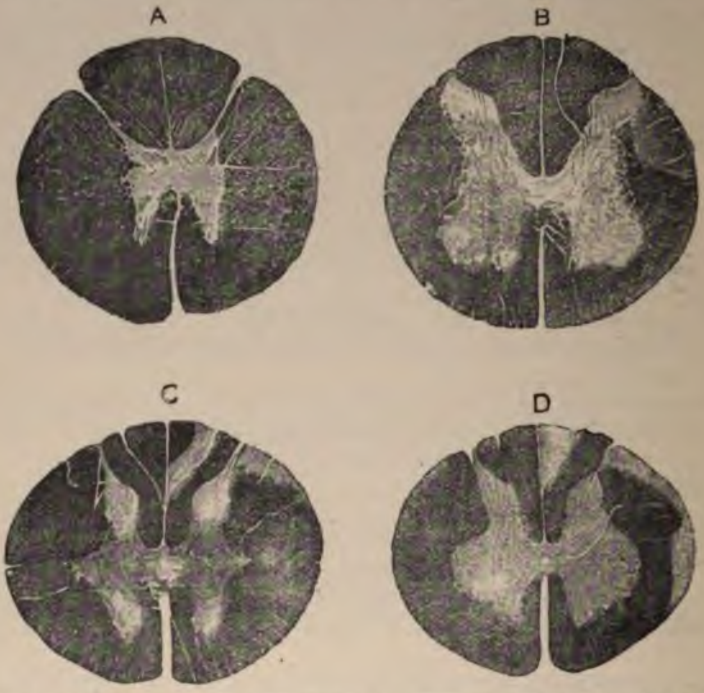

FIG. 452.—The above diagrams are reproductions of photo-micrographs from the spinal cord of a monkey, in which the operation of left hemisection had been performed some weeks previously (Mott.) The sections were stained by Weigert's method, by which the grey matter is bleached, while the healthy white matter remains dark blue. The degenerated tracts are also bleached. A is a section of the cord in the thoracic region below the lesion; the crossed pyramidal tract is degenerated. B is a section lower down in the lumbar enlargement; the degenerated pyramidal tract is now smaller. C is a section in the thoracic region some little distance above the lesion. The degenerated tracts seen are in the outer part of Goll's column, and in the direct cerebellar tract. D is a section higher up in the cervical region; the degeneration in Goll's column now occupies a median position; the degenerations in the direct cerebellar tract, and in the tract of Gowers, are also well shown. Notice that in all cases the degenerated traces are on the same side as the injury.

In the lumbar enlargement the grey matter again bears a very large proportion to the whole size of the transverse section, but its posterior cornua are shorter and blunter than they are in the cervical region. The grey commissure is short and extremely narrow. The cord is circular on transverse section.

At the upper part of the conus medullaris, which is the portion of the cord immediately below the lumbar enlargement, the grey substance occupies nearly the whole of the transverse section, as it is only invested by a thin layer of white sub-

stance. This thin layer is wanting in the neighbourhood of the posterior nerve-roots. The grey commissure is extremely thick.

At the level of the fifth sacral nerve **the grey matter is also in excess, and the central canal is enlarged, appearing T-shaped in section ; whilst in the** ***upper portion of the filum terminale*** **the grey matter is uniform in shape without any central canal.**

CHAPTER XLIII

THE BRAIN

A STUDENT'S first glance at a brain, or at such a drawing of it as is given in fig. 453, will be sufficient to convince him of its complicated structure. We shall devote this and a few succeeding chapters to anatomical considerations, before passing on to the study of its physiology.

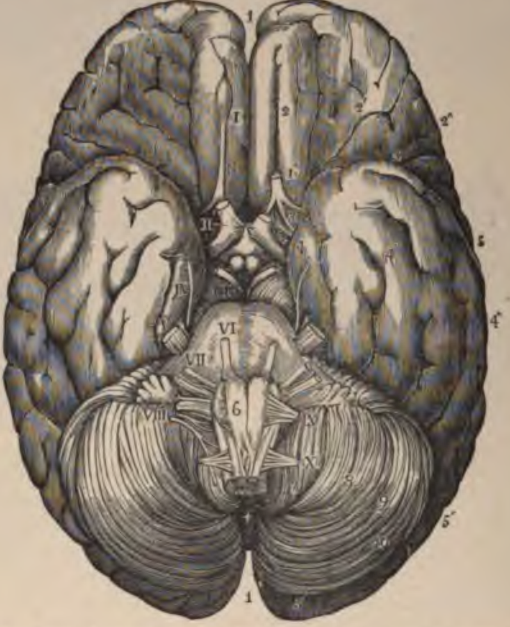

FIG. 453.—Base of the brain. 1, superior longitudinal fissure; 2, 2', 2'', anterior cerebral lobe; 3, fissure of Sylvius, between anterior and 4, 4', 4'', middle cerebral lobe; 5, 5', posterior lobe; 6, medulla oblongata; the figure is in the right anterior pyramid; 7, 8, 9, 10, the cerebellum; +, the inferior vermiform process. The figures from I. to IX. are placed against the corresponding cerebral nerves; III. is placed on the right crus cerebri. VI. and VII. on the pons Varolii; X. the first cervical or suboccipital nerve. (Allen Thomson.) ½.

At the lowest part of the brain (fig. 454), continuing the spinal cord upwards, is the *medulla oblongata* or *bulb* (D). Next comes the *pons Varolii* (C), very appropriately called the bridge, because in it are the connections between the bulb and the upper regions of the brain, and between the *cerebellum* or small brain (B) and the rest of the nervous system.

The *mid-brain* comes next (*a*, *b*), and this leads into the peduncles or crura of the *cerebrum* (A), the largest section of the brain.

Through the brain runs a cavity filled with cerebro-spinal fluid (see p. 178), and lined by ciliated epithelium; this is continuous with the central canal of the spinal cord. In the brain, however, it does not remain a simple canal, but is enlarged at intervals into what are called the **ventricles.** There is one ventricle in each half or hemisphere of the cerebrum; these are called the *lateral ventricles*, they open into the *third ventricle*, which is in the middle line; and then a narrow canal (*aqueduct of Sylvius*) leads from this to the *fourth ventricle*, which is placed on the back of the bulb and pons, which form its floor; its roof is formed partly by the overhanging cerebellum, partly by pia mater. This piece of pia mater is pierced by a hole (*Foramen of Magendie*), and so the cerebro-spinal fluid in the interior of the cerebro-spinal cavity is continuous with that which bathes the external surface of brain and cord in the sub-arachnoid space. The fourth ventricle leads into the central canal of the spinal

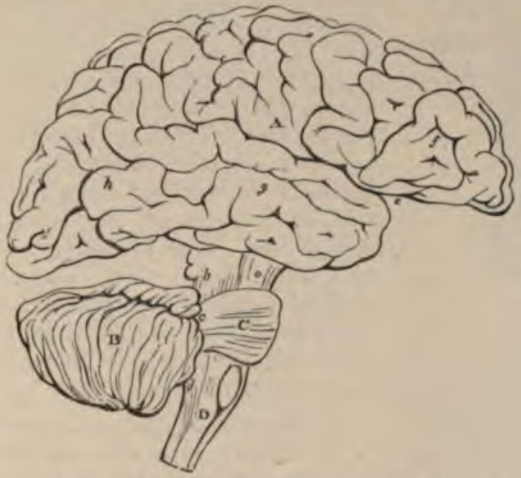

FIG. 454.—Plan in outline of the brain, as seen from the right side. ½. The parts are represented as separated from one another somewhat more than natural, so as to show their connections. A, cerebrum; *f*, *g*, *h*, its anterior, middle, and posterior lobes; *e*, fissure of Sylvius; B, cerebellum; C, pons Varolii; D, medulla oblongata; *a*, peduncles of the cerebrum; *b*, *c*, *d*, superior, middle, and inferior peduncles of the cerebellum. (From Quain).

cord. The fifth ventricle in the central structures of the brain does not communicate with the others.

Speaking generally, there are two main collections of grey matter—that on the surface, and that in the interior bordering on the cerebro-spinal cavity, and subdivided into various masses (floor of fourth ventricle, corpora striata, optic thalami, etc.), whose closer acquaintance we shall make presently.

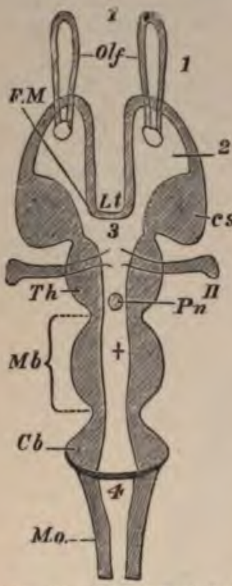

FIG. 455.—Diagrammatic horizontal section of a vertebrate brain. The figures serve both for this and the next diagram. *Mb*, mid-brain: what lies in front of this is the fore-, and what lies behind, the hind-brain; *Lt*, lamina terminalis; *Olf*, olfactory lobes; *Hmp*, hemispheres; *Th. E*, thalamencephalon; *Pn*, pineal gland; *Py*, pituitary body; *F.M.*, foramen of Munro; *cs*, corpus striatum; *Th*, optic thalamus; *CC*, crura cerebri: the mass lying above the canal represents the corpora quadrigemina; *Cb*, cerebellum; *M.o.*, medulla oblongata; *I—IX*, nine pairs of cranial nerves; 1, olfactory ventricle; 2, lateral ventricle; 3, third ventricle; 4, fourth ventricle; +, iter a tertio ad quartum ventriculum, or aqueduct of Sylvius. (Huxley.)

In the fœtus the central nervous system is formed by an infolding of a portion of the surface epiblast. This becomes a tube of nervous matter, which loses all connection with the surface of the body, though later in life this is in a sense re-established by the nerves that grow from the brain and cord to the surface. The anterior end of this tube becomes greatly thickened, to form the brain, its cavity becoming the cerebral ventricles; the rest of the tube becomes the spinal cord. The primitive brain is at first subdivided into three parts, the *primary cerebral vesicles;* the first and third of these again-subdivide, so that there are ultimately five divisions, which have received the following names:—

1. **Pros-encephalon,** or *fore brain.* This is developed into the cerebrum with the corpora striata. It encloses the lateral ventricles.

2. **Thalam-encephalon,** or *twixt brain.* This is developed into the parts including the optic thalami, which enclose the third ventricle.

3. **Mes-encephalon,** or *mid brain,* consists of the parts which enclose the aqueduct of Sylvius—namely, the corpora quadrigemina, which form its dorsal, and the crura cerebri, which form its ventral aspect.

4. **Ep-encephalon,** or *hind brain,* which forms the cerebellum and pons.

5. **Met-encephalon,** or *after brain,* which forms the bulb or medulla oblongata.

Figs. 455 and 456 represent a diagrammatic view of a vertebrate brain; the attachment of the pineal gland, pituitary body, and olfactory (I) and optic (II) nerves is also shown.

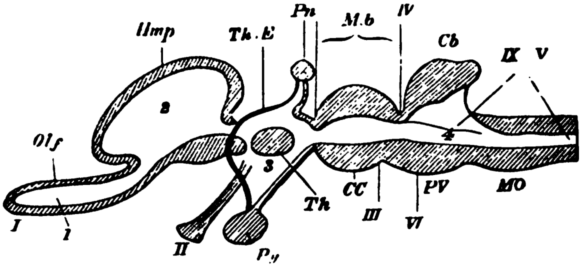

FIG. 456.—Longitudinal and vertical diagrammatic section of a vertebrate brain. Letters as before *PV*, pons Varolii. Lamina terminalis is represented by the strong black line joining *Pn* and *Py*. (Huxley.)

CHAPTER XLIV

STRUCTURE OF THE BULB, PONS, AND MID-BRAIN

WE may study the bulb and pons by examining first the anterior or ventral, then the posterior or dorsal aspect, and last of all the interior.

Anterior Aspect.

The bulb is seen to be shaped, like an inverted truncated cone, larger than the spinal cord, and enlarging as it goes up until it terminates in the still larger pons (fig. 457, *p*). In the middle line is a groove, which is a continuation upwards of the anterior median fissure of the spinal cord; the columns of the bulb are, speaking roughly, continuations upwards of those of the cord, but there is a considerable rearrangement of the fibres in each. Thus the prominent columns in the middle line, called the *pyramids* (*a a*), are composed of the pyramidal fibres, which in the spinal cord are situated principally in the lateral columns of the opposite side (crossed pyramidal tracts). The decussation or crossing of the pyramids (*b*) occurs at their lower part: a small collection of the pyramidal fibres is, however, continued down the cord in the anterior column of the same side of the cord (direct pyramidal tract): these cross at different levels in the cord.

On the outer side of each pyramid is an oval prominence (*c c*), which is not represented in the spinal cord at all. These are called the *olivary bodies* or *olives;* they consist of white matter outside, with grey and white matter in their interior.

The *restiform bodies* at the sides (*d d*) are the continuation upwards of those fibres from cord and bulb which enter the cerebellum, and the upper part of each restiform body is called the *inferior peduncle of the cerebellum.**

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* Each half of the cerebellum has three peduncles: inferior, middle, and superior.

Posterior Aspect.

Fig. 458 shows a surface view of the back of the bulb, pons, and mid-brain. Again we recognise some of the parts of the spinal cord continued upwards, though generally with new names, and again we see certain new structures.

The posterior median fissure is continued upwards, and on each side of it is the prolongation upwards of the posterior column of the cord. The column of Goll is now called the *Funiculus gracilis*, and the column of Burdach the *Funiculus cuneatus.*

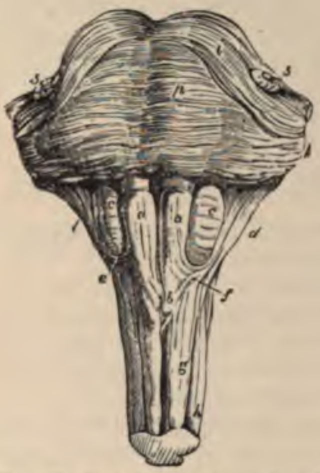

FIG. 457.—Ventral or anterior surface of the pons Varolii, and medulla oblongata. *a*, *a*, pyramids; *b*, their decussation; *c*, *c*, olivary bodies; *d*, *d*, restiform bodies; *e*, arcuate fibres; *f*, fibres passing from the anterior column of the cord to the cerebellum; *g*, anterior column of the spinal cord; *h*, lateral column; *p*, pons Varolii; *i*, its upper fibres; 5, 5, roots of the fifth pair of nerves.

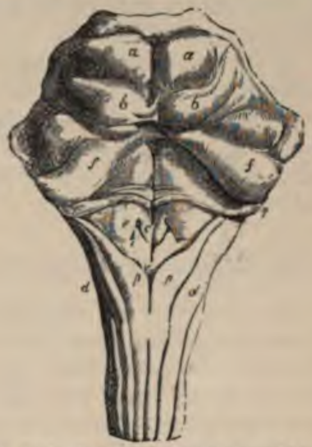

FIG. 458.—Dorsal or posterior surface of the pons Varolii, corpora quadrigemina, and medulla oblongata. The peduncles of the cerebellum are cut short at the sides. *a*, *a*, the upper pair of corpora quadrigemina; *b*, *b*, the lower; *f*, *f*, superior peduncles of the cerebellum; *c*, eminence connected with the nucleus of the hypoglossal nerve: *e*, that of the glosso-pharyngeal nerve; *i*, that of the vagus nerve; *d*, *d*, restiform bodies; *p*, *p*, posterior columns; *v*, *v*, groove in the middle of the fourth ventricle, ending below in the calamus scriptorius; 7, 7, roots of the auditory nerves.

The two funiculi graciles lie at first side by side, but soon diverge and form the two lower boundaries of a diamond-shaped space called the *floor of the fourth ventricle;* this is made of grey matter; the central canal of the cord gets nearer and nearer to the dorsal surface of the bulb, till at last it opens out on the back of the bulb, and its surrounding grey matter is spread out to form the floor of the fourth ventricle. The two upper boundaries of the diamond-shaped space are made by the superior peduncles of the cerebellum, which contain fibres going up through the mid-brain to the cerebrum. The middle peduncles of the cerebellum are principally made up of fibres running from one cerebellar hemisphere towards the other through the pons.

Running down the centre of the floor of the fourth ventricle is a shallow groove; on each side of this is a rounded longitudinal eminence called the *eminentia teres;* running across the middle of the floor are a number of fibres (the *striæ acousticæ*), which join the auditory nerve.

In the upper part of the diagram, the mid-brain, with the *corpora quadrigemina* (*a a*, *b b*), is shown. Here there is once more a canal which penetrates the substance of the mid-brain, and is called the *aqueduct of Sylvius*, or the *iter a tertio ad quartum ventriculum;* it leads, as its second name indicates, from the third to the fourth ventricle.

The Internal Structure of the Bulb, Pons, and Mid-Brain.

The structure of the interior of these parts is complex, and the complexity arises from the circumstance that here we have to deal not only with parts running upwards from cord to brain, or down from brain to cord, but also with a considerable amount of grey matter in which some of the white tracts terminate, or from which new tracts issue. The most important stretch of grey matter is that which appears on the floor of the fourth ventricle, and which is continued upwards around the Sylvian aqueduct, and downwards into the spinal cord; here are situated groups of nerve-cells, which are spoken of as centres, or nuclei. The most important of these are those which are connected to the cranial nerves. There are altogether twelve pairs of cranial nerves, and of these the last ten pairs originate from the floor of the fourth ventricle or the neighbouring grey matter.

The following is a list of the cranial nerves:—

1. *Olfactory.*—This is the nerve of smell.
2. *Optic.*—This is the nerve of sight.
3. *Motor oculi*
4. *Trochlear*
6. *Abducens*
} These three nerves supply the muscles of the eyeball.

5. *Trigeminal.*—This is the great sensory nerve of the face and head. Its smaller motor division supplies the muscles of mastication and a few other muscles also.

7. *Facial.*—This is mainly the motor nerve of the face muscles.

8. *Auditory.*—This is divided into two parts, one of which, called the *cochlear* nerve, is the true nerve of hearing, and is distributed to

the cochlea of the internal ear; the other division, called the *vestibular* nerve, is distributed to the vestibule and semi-circular canals of the internal ear.

9. *Glossopharyngeal.*—This is a mixed nerve; its motor fibres pass to certain of the pharyngeal muscles; its sensory fibres are mainly concerned in the sense of taste.

10. *Vagus or pneumogastric.*—This is a nerve with varied efferent and afferent functions; its branches pass to pharynx, larynx, œsophagus, stomach, lungs, heart, intestines, liver and spleen. Most of these functions we have already studied in connection with these organs.

11. *Spinal accessory.*—The internal branch of this nerve blends with the vagus, and its larger external division supplies the trapezius and the sterno-mastoid muscles.

12. *Hypoglossal.*—This is the motor nerve to the tongue muscles.

A mere enumeration of the nerves connected to the bulb shows how supremely important this small area of the brain is for carrying on the organic functions of life. It contains centres which regulate deglutition, vomiting, the secretion of saliva, etc., respiration, the heart's movements, and the vaso-motor nerves.

When we further consider that the various centres are connected by groups of association fibres, we at once realise the reason for the complexity of the structures where all this busy traffic takes place.

In the enumeration of the cranial nerves, it will be noticed that many of them are either wholly motor or wholly sensory, and that some of them, like the spinal nerves, have a double function. The motor nerve fibres start as axons from the groups of nerve-cells in the grey matter of this region, just as the motor fibres in the spinal nerves originate from the cells of the spinal grey matter. There is a corresponding resemblance in the origin of the sensory fibres of the cranial and spinal nerves. In the latter, it will be remembered, they originate as outgrowths from the cells of the spinal ganglia, one branch growing to the periphery, and the other to the spinal cord, where it terminates after a more or less extended course by forming synapses with the cells of the grey matter. In the cranial nerves they have a corresponding origin in peripheral ganglia, and those branches which grow towards the bulb terminate by arborising around special groups of cells spoken of as the sensory nuclei.

The following diagram (fig. 456) roughly indicates the position of these nuclei; the motor nuclei are coloured blue, and the sensory red. It must, however, be clearly recognised that while the motor nuclei are true centres of origin, that the so-called sensory nuclei are groups of cells around which the entering sensory fibres arborise; these cells do not give origin to the axons of the sensory nerves. After we have studied the internal structure of the bulb we shall be able to return once more to the cranial nerves, in order that we consider their origin and function in greater detail.

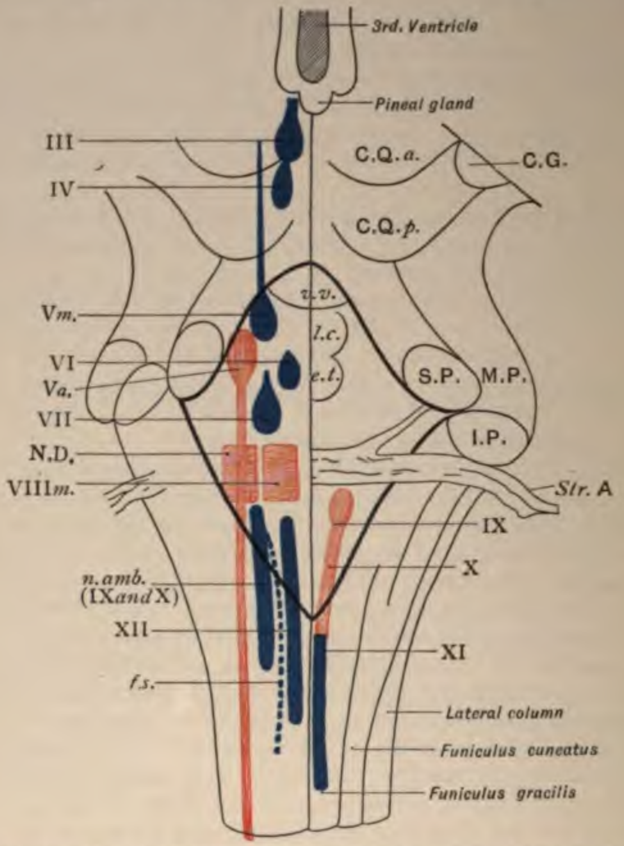

FIG. 459.—Diagram to show the position of the nuclei of the cranial nerves (after Sherrington). The medulla and pons are viewed from the dorsal aspect, the cerebrum and cerebellum having been cut away. The nuclei (sensory coloured red, and motor blue) are represented as being seen through transparent material. C.Q. *a.*, anterior corpus quadrigeminum; C.Q. *p.*, posterior corpus quadrigeminum; C.G., corpus geniculatum; *v.v.*, value of Vieussens; *l.c.*, locus cœruleus; *e.t.*, eminentia teres; *str.* A., striæ acousticæ. S.P., M.P., and I.P., superior middle and inferior cerebellum peduncles respectively cut through. The numerals III. to XII. indicate the nuclei of the respective cranial nerves, all shown on the left side except the accessory-vago-glossopharyngeal IX., X., XI., which to avoid confusion is placed on the right side. V*m.* is the motor nucleus of the fifth nerve; V*d.*, the sensory nucleus of the same nerve with its long descending root; VIII*m.*, the median nucleus of the auditory nerve; N.D. Nucleus of Deiters; *n. amb.* nucleus ambiguus. The position of the descending root of the ninth and tenth (fasciculus solitarius) is also indicated (*f. s.*).

But this diagram will give a general idea of the positions of the nuclei. It will be noticed that the so-called sensory nuclei (coloured red) are in the minority; they comprise the sensory nucleus of the fifth nerve with its long descending (formerly called ascending) root, the nuclei of the eighth nerve (only one of which, VIII*m.*, is seen in the diagram), and the glossopharyngeal and vagal portions of a long strand of nerve-cells called the *combined nucleus* of the ninth, tenth, and eleventh nerves. The remaining nuclei (coloured blue) are efferent, and may be principally arranged into two groups:—(1) the nuclei of the third, fourth, sixth, and twelfth nerves, which are close to the middle line; and (2) the motor nucleus of the fifth, the nucleus of the seventh, and the nucleus ambiguus (motor nucleus of the ninth and tenth nerves) which form a line more lateral in position.

It should be added that van Gehuchten has shown that, except a few fibres of the third, and the whole of the fourth nerves, none of the fibres of the cranial nerves cross to the opposite side.

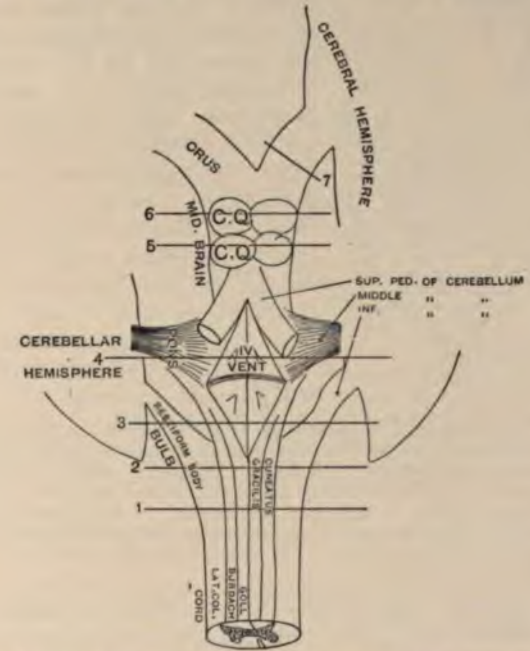

FIG. 460.—Diagrammatic representation of dorsal aspect of medulla, pons, and mid-brain.

The first two pairs of cranial nerves, the olfactory and the optic, will be studied in connection with smell and vision later on.

We can now pass to the consideration of transverse sections of this part of the central nervous system. We will limit ourselves to seven, the level of which is indicated in the above diagram (fig. 460). The cerebellum has been bisected into two halves and turned outwards, its upper peduncles having been cut through to render the parts more evident. The position of our seven sections is indicated by the transverse lines numbered 1 to 7.

First section.—This is taken at the lowest level of the bulb, through the region of the decussation of the pyramids. The similarity to the cervical cord will be at once recognised; the passage of the pyramidal fibres (P) from the anterior part of the bulb to the crossed pyramidal tract of the opposite side of the cord cuts off the tip of anterior horn (A), which in sections higher up appears as an isolated mass of grey matter, called the *lateral nucleus* (fig. 462, *nl*). The V formed by the two posterior horns is opened out, and thus the grey matter with the central canal is brought nearer to the dorsal aspect of the bulb; the tip of the cornu swells out to form the *substantia gelatinosa of Rolando* (R), which causes a prominence on the surface called the *tubercle of Rolando;* G and C are the *funiculi gracilis* and *cuneatus* respectively, the continuations upwards of the columns of Goll and Burdach.

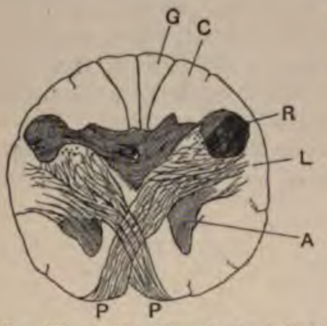

FIG. 461.—Section through the bulb at the level of the decussation of the pyramids. G, funiculus gracilis, continuation of column of Goll; C, funiculus cuneatus, continuation of column of Burdach; R, substantia gelatinosa of Rolando, continuation of posterior horn of spinal cord; L, continuation of lateral column of cord; A, remains of part of the anterior horn, separated from the rest of the grey matter by the pyramidal fibres P, which are crossing from the pyramid of the medulla to the posterior part of the lateral column of the opposite side of the cord.
(After L. Clarke.)

Many of the fibres of the pyramidal tract terminate in the mid-brain and pons, hence this tract is reduced in size when it reaches the bulb. The pyramidal fibres on their long journey give off collaterals to the cortex cerebri, the basal ganglia of the cerebrum, the substantia nigra of the mid-brain, the nuclei pontis of the pons, and lower down in the cord to the base of its posterior horn. They, however, do not give off collaterals to the motor nuclei of the cranial nerves on their passage through the bulb (Schäfer). The only collaterals given off in this region are a few to the olivary nuclei.

Second section (fig. 462).—This is taken through the upper part of the decussation. Beginning in the middle line at the top of the diagram, we see first the posterior median fissure (*p.m.f.*), below which is the grey matter enclosing the central canal (*c.c.*), and containing the nuclei of the eleventh and twelfth nerves; the funiculus gracilis (*f.g.*) comes next, and then the funiculus cuneatus (*f.c.*); these two funiculi have now grey matter in their interior: these masses of grey matter are called respectively *nucleus gracilis* (*n.g.*) and *nucleus cuneatus* (*n.c.*); the fibres which have ascended the posterior columns of the cord terminate by arborising around the cells of this grey matter; the fibres from the lower part of the body end in the nucleus gracilis, and those from the upper part of the body in the nucleus cuneatus. These nuclei form a most important position of relay in the course of the afferent fibres from cord to brain. The new fibres (the second relay of the sensory spinal path) arising from the cells of these nuclei pass in a number of different directions, and

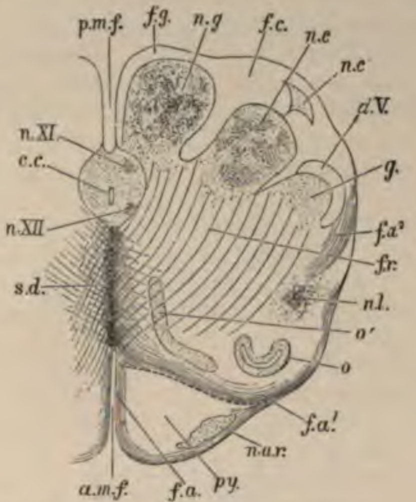

FIG. 462.—Transverse section of the medulla oblongata in the region of the superior decussation. *a.m.f.*, anterior median fissure; *f.a.*, superficial arcuate fibres; *py.*, pyramid; *n.a.r.*, nuclei of arcuate fibres; *f.a*^{1}, deep arcuate fibres becoming superficial; *o*, *o'*, lower end of olivary nucleus; *n.l.*, nucleus lateralis; *f.r.*, formatio reticularis; *f.a*^{2}, arcuate fibres proceeding from the formatio reticularis; *g*, substantia gelatinosa of Rolando; *d.V.*, descending root of fifth nerve; *f.c.*, funiculus cuneatus; *n.c.*, nucleus cuneatus; *n.c.'*, external cuneate nucleus; *n.g.*, nucleus gracilis; *f.g.*, funiculus gracilis; *p.m.f.*, posterior median fissure; *c.c.*, central canal surrounded by grey matter, in which are *n.XI.*, nucleus of the eleventh and *n.XII.*, nucleus of the twelfth nerve; *s.d.*, superior decussation (decussation of fillet). (Modified from Schwalbe.)

break up the rest of the grey matter into what is called the *formatio reticularis.*

The nucleus gracilis and nucleus cuneatus are often spoken of as the *posterior column nuclei;* they do not receive all the ascending branches of the posterior root fibres, for a number of these branches have already entered the grey matter and arborised amongst its cells in the spinal cord itself. The cells of the posterior column nuclei are of moderate size, and their axons pass as *internal arcuate fibres* into the reticular formation between the two olivary bodies, which is known as the *inter-olivary layer.* They cross the median raphe dorsal to the pyramids, and then turn upwards towards the upper parts of the brain, and so constitute what is known as the *fillet.* In the higher parts of the bulb and pons, this tract is reinforced by fibres from the cells of the sensory nuclei of the cranial nerves. The fillet becomes a longitudinal bundle, which passes upwards to various parts of the cerebrum, but the sensory impulses go through one or more cell-stations (positions of relay) before they ultimately arrive at the cortex. We now see that the brain has a crossed relationship to the body, the left half of the brain governing the right half of the body, and *vice versâ*, both as regards motion and sensation; the motor fibres mostly cross at the decussation of the pyramids, some few (those in the direct pyramidal tract) crossing at lower levels in the cord; the sensory fibres mostly cross at the decussation of the fillet, though some few cross at lower levels in the cord, soon after their entrance into the cord by the posterior nerve-roots.

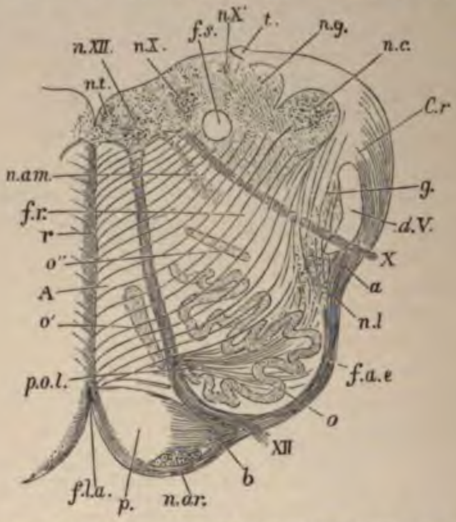

FIG. 463.—Section of the medulla oblongata at about the middle of the olivary body. *f.l.a.*, anterior median fissure; *n.ar.*, nucleus arcuatus; *p*, pyramid; *XII.*, bundle of hypoglossal nerve emerging from the surface; at *b*, it is seen coursing between the pyramid and the olivary nucleus, *o*; *f.a.e.*, external arcuate fibres; *n.l.*, nucleus lateralis; *a.*, arcuate fibres passing towards restiform body, partly through the substantia gelatinosa, *g.*, partly superficial to the descending root of the fifth nerve, *d.V.*; *X.*, bundle of vagus root emerging; *f.r.*, formatio reticularis; *C.r.*, corpus restiforme, beginning to be formed, chiefly by arcuate fibres, superficial and deep; *n.c.*, nucleus cuneatus; *n.g.*, nucleus gracilis; *t*, attachment of the ligula; *f.s.*, funiculus solitarius; *n.X.*, *n.X.'*, two parts of the vagus nucleus; *n.XII.*, hypoglossal nucleus; *n.t.*, nucleus of the funiculus teres; *n.am.*, nucleus ambiguus; *r.*, raphe; *A.*, continuation of the anterior column of cord; *o'*, *o''*, accessory olivary nucleus; *p.o.l.*, pedunculus olivæ. (Modified from Schwalbe.)

Other points to be noticed in the section are the substantia gelatinosa of Rolando (*g*) (remains of posterior cornu of the cord), now separated from the surface by the descending root of the fifth nerve (*d. V.*); the lateral nucleus (*n l*) (remains of the anterior cornu of the cord); the lower part of the grey matter of the olivary body (*o, o'*), and most anteriorly the *pyramid* (*py*).

Third section.—This (fig. 463) is taken at about the middle of the olivary body, and passes also through the lower part of the floor of the fourth ventricle. The central canal has now opened out into the fourth ventricle, and the grey matter on its floor contains the nuclei of the twelfth and tenth nerves; bundles of the fibres of these nerves course through the substance of the bulb, leaving it at the places indicated in the diagram.

The nucleus gracilis, nucleus cuneatus, are pushed into a more lateral position, and higher up are replaced by small masses of grey matter mingled with nerve-fibres (*nucleus posterior*); the *restiform body* (*C.r.*) now forms a well-marked prominence, and the olivary body is well seen with its *dentate nucleus;* from the open mouth of this corrugated layer of grey matter a large number of fibres issue, and passing through the raphé, course as internal arcuate fibres to the opposite restiform body, and thus to the cerebellum; some pass to the restiform body of the same side; the continuation of the direct cerebellar tract of the cord also passes into the restiform body. Its fibres terminate by arborisations round Purkinje's cells in the *vermis* of the cerebellum. The continuation of the tract of Gowers lies just dorsal to the olivary body. The *funiculus solitarius* and *nucleus ambiguus*, also seen in this section, will be more fully considered in our account of the origin of the ninth and tenth cranial nerves.

Fourth section (fig. 464).—This is taken through the middle of the pons, and shows much the same kind of arrangement as in the upper part of the bulb. The general appearance of the section is, however, modified by a number of transversely coursing bundles of fibres, most of which are passing from the cerebellar hemispheres to the raphe, and form the middle cerebellar peduncles. Intermingled with these is a considerable amount of grey matter (*nuclei pontis*).

From the cells of the nuclei pontis, many of the fibres of the middle peduncle take origin, and many fibres and collaterals of the pyramidal tract arborise around them. The continuation of the pyramids (*py*) is embedded between these transverse bundles. The pyramidal fibres which terminate in the pons are situated postero-laterally, and are spoken of as *cortico-pontine* in contradistinction with those of the pyramidal tract proper (*cortico-spinal*) which pass down through the bulb to the cord.

The pyramidal bundles are separated from the reticular formation by deeper transverse fibres, which constitute what is known as the *trapezium* (*t*). These fibres belong to a different system, and form part of the central auditory path; some of them connect the auditory nuclei of the two sides together. The larger olivary nucleus is no longer seen, but one or two small collections of grey matter (*o.s.*) represent it and constitute the *superior olivary nucleus*. These as well as a collection of nerve-cells in the trapezium (*nucleus of the trapezium*) are connected with fibres of the trapezium, while some of their axons pass into the adjacent lateral part of the fillet.

The *nucleus of Deiters* (*n. VIII*, fig. 464) begins to appear in the upper part of the bulb, and extends into the pons; it lies near the floor of the ventricle, a little mesial to the restiform body. The nerve-fibres connected with its cells pass towards the middle line, and enter the *posterior longitudinal bundle*, which is more clearly seen in the two next sections (fig. 465). This bundle of fibres connects Deiters' nucleus, the nucleus of the third and sixth nerves, and the anterior horn cells of the spinal cord. The fibres which pass into it from Deiters' nucleus bifurcate, one branch passing upwards to arborise around the cells mainly of the oculo-motor nucleus of the opposite side; the other extends downwards through the bulb into the cord, where they are found in the antero-lateral descending tract of each side. They terminate by synapses around the anterior horn cells.

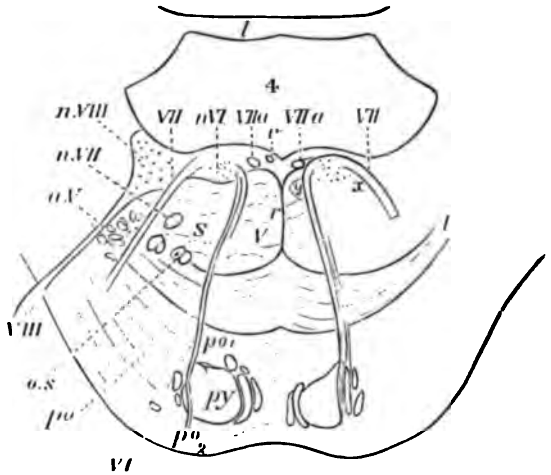

FIG. 464. Section across the pons, about the middle of the fourth ventricle. *py.*, pyramidal bundles; *po.*, transverse fibres passing po_1 behind, and po_2, in front of *py*; *r.*, raphe; *o.s.*, superior olive; *a.V.*, bundles of motor root of *V.* nerve enclosed in a prolongation of the substance of Rolando; *t*, trapezium; *VI.*, the sixth nerve, *n. VI.*, its nucleus; *VII.*, facial nerve; *VII. a.*, intermediate portion, *n. VII.*, its nucleus; *VIII.*, auditory nerve, *n. VIII.*, Deiters' nucleus formerly called the lateral nucleus of the auditory. (After Quain.)

This bundle receives in addition to the fibres from Deiters' nucleus, other fibres from the sensory nucleus of the fifth nerve, and from large cells in the reticular formation of mid-brain, pons, and bulb.

The nerves which are connected with the grey matter of this region of the pons are the sixth, seventh, and eighth, as shown in the diagram. The nuclei in connection with the fifth nerve are higher up, where the floor of the ventricle is again narrowing. At last, in the region of the mid-brain, we once more get a canal (Sylvian aqueduct) which corresponds to the central canal of the spinal cord.

Fifth and Sixth sections are taken through the mid-brain, and are drawn on a smaller scale than the others we have been examining; they represent the actual size of the sections obtained from the human subject.

Near the middle is the *Sylvian aqueduct*, with its lining of ciliated epithelium. In the grey matter which surrounds it are large nerve-cells from which the fourth nerve, and higher up the third nerve, originate; the fibres of the third nerve are seen issuing from these in fig. 465, B., III. The reticular formation of the pons is continued up into the mid-brain, and is called the *tegmentum*. It is composed of both longitudinal and transverse bundles of fibres intermingled with grey matter. Its transverse fibres include those of the superior peduncles of the cerebellum which decussate in the middle line (fig. 465, A., S.C.P.). These originate from the cells of the dentate nucleus of the cerebellum; after decussation they bifurcate, the ascending branches being lost in the collection of nerve-cells in the tegmentum known as the *tegmental* or *red nucleus*, while the descending branches turn downwards in the reticular formation. The axons from the cells of the red nucleus run downwards and form Monakow's bundle, or the prepyramidal tract which we have already seen in the spinal cord.

Another important longitudinal bundle in the tegmentum is the fillet. This, we have seen, is the longitudinal continuation of the internal arcuate fibres, which, starting from the cells of the posterior column nuclei of the opposite side, form the second relay on the sensory path; to these fibres others are added which originate from other masses of grey matter in bulb and pons. In the mid-brain the fillet splits into three bundles, termed the *lateral*, the *upper*, and the *mesial fillet*.

(1) *The lateral fillet* is chiefly formed by fibres derived from the accessory auditory, the inferior olivary, and trapezoid nuclei of the opposite side. Some of its fibres terminate by synapses around a new collection of cells (the *lateral fillet nucleus*); their axons pass inwards towards the raphe. The rest of its fibres can be traced to the grey matter of the inferior corpora quadrigemina.

(2) *The upper fillet* consists of fibres which go to the superior corpora quadrigemina and partly to the tegmental region of the mid-brain and optic thalamus.

(3) *The mesial fillet* goes on through the tegmentum of the crus cerebri, and its fibres terminate around the cells of the optic thalamus, and the subthalamic region. From here fresh axons forming a new relay continue the afferent impulses to the cortex of the cerebrum.

The mesial fillet is the important link in this region between the sensory *spinal* nerves and the part of the brain which is the seat of those processes we call sensations. But most of the fibres which continue the sensory path of the *cranial* nerves form another less well-defined tract (*the central tract of the sensory cranial nerves*) which lies dorsal to the fillet, but terminates like it in the subthalamic region and optic thalamus, whence a new relay carries on the impulses to the cortex.

Ventral to the tegmentum is a layer of grey matter, of which the cells are deeply pigmented; hence it is called the *substantia nigra* (S.N.). This receives many collaterals from the pyramidal bundles.

The white matter on the ventral side of this is known as the *crusta* (*Cr*) or *pes*. It is here that the pyramidal bundles are situated; these occupy its middle three-fifths (*Py*). The mesial fifth is occupied by fibres passing from the frontal region of the cerebrum to the pons, and thence, it is believed, to the cerebellum; hence they are called *fronto-cerebellar* fibres. The fibres occupying the lateral fifth are usually spoken of as *temporo-occipital cerebellar* fibres, but there is no certainty as yet regarding their origin or functions.

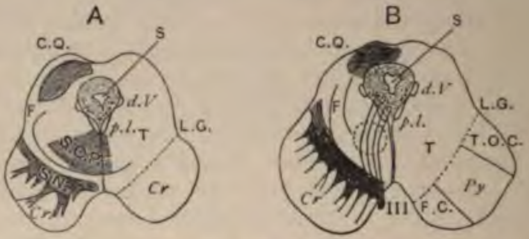

FIG. 465.—Outline of two sections across the mid-brain: A, through the middle of the inferior; B, through the middle of the superior corpora quadrigemina, C.Q. *Cr.*, crusta; S.N., substantia nigra—shown only on one side; T, tegmentum; S, Sylvian aqueduct, with its surrounding grey matter; L.G., lateral groove; *p.l.*, posterior longitudinal bundle; *d.V.*, descending root of the fifth nerve; S.C.P., superior cerebellar peduncle; F, fillet; III., third nerve. The dotted circle in B represents the situation of the tegmental nucleus. In B the three divisions of the crusta are indicated on one side. The pyramidal fibres (*Py*) are in the middle, and the fronto-cerebellar (F.C.) and temporo-occipital cerebellar (T.O.C.) at the sides. (After Schäfer.)

The *corpora quadrigemina* are formed mainly of grey matter; from each superior corpus a bundle of white fibres passes upwards and forwards to the geniculate bodies, eventually joining the optic tract of the same side. The white layer on the surface of the grey matter of the C. quadrigemina is derived from the optic tract; these fibres come from the retina, and terminate by arborising around the cells of the grey matter of the C. quadrigemina.

The cells of the grey matter of the corpora quadrigemina differ greatly in form and size; the destination of their axons is not precisely known, but some pass ventralwards, cross at the raphe, and constitute the *fountain decussation of Meynert;* after decussation they form the main mass of the *ventral longitudinal bundle;* this gives off collaterals to the nuclei of the three nerves that supply the eye muscles, and then runs ventro-laterally to the posterior longitudinal bundle, with which its fibres ultimately mix in the antero-lateral descending tract of the spinal cord.

Seventh section.—This is through the crus. It is made up of *crusta* (which contains the motor fibres), *tegmentum* (which contains the sensory fibres, especially the bundle called the mesial fillet), and the *substantia nigra*, the grey matter which separates them.

The destination of one of the spinal cord tracts we have not yet mentioned; this is the tract of Gowers. This is continued up through the ventral part of the pons lateral to the pyramidal bundles; when it reaches the superior cerebellar peduncles the main part of the tract takes a sharp backward turn and enters the middle lobe or *vermis* of the cerebellum by the superior peduncle and superior medullary velum. Some of the fibres of the tract are continued, however, into the corpora quadrigemina.

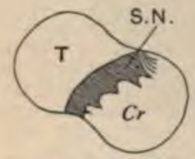

FIG. 466.—Section through crus of cerebrum. *Cr*, crusta; S.N., substantia nigra; T, tegmentum.

The Tracts of the Bulb, Pons, and Mid-Brain.

In the preceding description we have had occasion to mention the main tracts which are seen in transverse section. It will now be convenient to summarise matters by enumerating them again as well as certain others which are of less importance, or concerning which we know less. The tracts may be divided into two main groups, those which are descending and those which are ascending.

Descending tracts.—The principal descending tract is (*a*) the *pyramidal tract.* This has already been sufficiently described, so also have (*b*) the *posterior* and (*c*) the *ventral longitudinal bundles.* The remaining tracts are:—

(*d*) *Monakow's bundle.*—These fibres start from the cells of the red nucleus, cross the raphe in Forel's fountain decussation; they eventually pass into the lateral column of the cord as the prepyramidal tract.

(*e*) *The ponto-spinal lateral tract* starts from the large cells of the formatio reticularis, and runs down the lateral portion of this formation through the pons and bulb. In the spinal cord the fibres, mixed with many others of different origin, lie in the lateral column between the grey matter and the tracts of Gowers and Monakow. They pass like the fibres of the posterior and ventral longitudinal bundles into the grey matter of the anterior cornu.

(*f*) *The vestibulo-spinal tract fibres* are similar in origin to those of the posterior longitudinal bundle; its fibres lie mixed with those of the two last-mentioned tracts, and their destination is the grey matter of the anterior horn.

(*g*) *The central tract of the tegmentum;* this is a distinct bundle which lies in the middle of the reticular formation, but its origin and destination are both unknown.

(*h*) Other longitudinal fibres of the tegmentum are (1) the *fasciculus retroflexus*, which passes obliquely from the ganglion of the trabecula (a collection of cells near the middle of the optic thalamus) to the interpeduncular ganglion of the opposite side (a collection of cells just where the peduncles diverge from the transverse fibres of the pons); (2) *Von Gudden's bundle*, which runs from the corpora mammillaria to end in the tegmentum; these fibres decussate, and their intercrossing together with that of Monakow's bundle constitutes the fountain decussation of Forel.

Ascending Tracts.—The most important of these are—(*a*) the tract of the *fillet*, and (*b*), the *central tract of the cranial sensory nerves.* We must also remember the fibres that connect the cord to the cerebellum ((*c*) *dorsal and* (*d*) *ventral cerebellar tracts*), and (*e*) the fibres that pass into the *restiform body* (inferior cerebellar peduncle) from the olivary body.

The *superior cerebellar peduncles* originate from the dentate nucleus of the cerebellum; we have already seen them converging to the middle line as they pass upwards, and decussating in the mid-brain at the level of the posterior C. quadrigemina; they terminate in the red nucleus of the tegmentum. Before they cross they give off branches which Cajal describes as forming a *descending cerebellar bundle*, which gives off collaterals to the motor nucleus of the fifth, the nucleus of the seventh, and perhaps to the nucleus ambiguus. One bundle of fibres in the superior cerebellar peduncle starts from cells in the optic thalamus, and conveys impulses downwards to the cerebellum.

Origins and Functions of the Cranial Nerves.

Having now studied the internal construction of these parts, we can take up more fully the origins and functions of the cranial nerves which originate there. The olfactory nerve is connected to the cerebrum, and will be considered with the sense of smell. The optic nerve will be studied with vision, though it is, as we have seen, immediately connected with the mid-brain.

The third, fourth, and sixth nerves are wholly motor, and supply the muscles of the eye. Gaskell discovered among the rootlets of the third and fourth nerves the vestiges of a degenerated and functionless ganglion, which indicates the previous existence of a sensory portion of these nerves.

The third nerve (*motor oculi*) arises in a group of nerve-cells in the grey matter on the side of the Sylvian aqueduct underneath the superior corpus quadrigeminum, and close to the middle line. The anterior part of this nucleus is composed of small cells from which small nerve-fibres originate for the ciliary muscle and sphincter of the iris (intrinsic muscles of the eyeball). These fibres correspond to the visceral fibres of a spinal nerve, and, like them, have a cell station, namely, in the ciliary ganglion. The posterior part of the nucleus is composed of larger cells, and these give rise to larger fibres which supply the following extrinsic eye-muscles:—superior rectus, inferior rectus, internal rectus, inferior oblique and levator palpebræ.

The fourth nerve (*trochlear*) takes origin from the grey matter immediately below the centre of the third, but slightly more lateral in position. It is situated underneath the inferior corpus quadrigeminum. It supplies the superior oblique muscle of the opposite eyeball.

The sixth nerve (*abducens*) arises from a centre beneath the eminentia teres in the upper part of the floor of the fourth ventricle near the middle line. It supplies the external rectus.

It is obviously necessary that the eye-muscles should work together harmoniously, that the two eyeballs should also be moved simultaneously and in corresponding directions, and that such movements should take place in accordance with the necessities of vision. This is provided for in the shape of association fibres which link the centres of the eye-muscles together. The principal association tracts are the posterior longitudinal bundle, which connects the nuclei of the third and sixth nerves, and the ventral longitudinal bundle which unites the optic nerves through the intermediation of the cells of the C. quadrigemina, with the nuclei of all these nerves. It should also be remembered that all the fibres of the fourth, and some of those of the third nerve decussate, in the middle line.

The fifth nerve (*trigeminal*) is a mixed nerve; it leaves the side of the pons in a smaller motor, and a larger sensory division. The former supplies the muscles of mastication, the tensors of the palate and tympanum, the mylo-hyoid, and the anterior belly of the digastric; the sensory division has upon it a ganglion called the Gasserian ganglion; it is the great sensory nerve of the face and head. The motor fibres arise from the motor nucleus (V*m*, fig. 459), which lies at the lateral edge of the upper part of the floor of the fourth ventricle, but a certain number of its fibres arise from cells in the lower part of the mid-brain and upper part of the pons; this long stretch of nerve-cells, indicated by the long blue tail in the diagram, is called the *accessory* or *superior motor nucleus* of the fifth. The sensory fibres arise from the cells of the Gasserian ganglion, which resemble in structure those of a spinal ganglion; one branch of each passes to the periphery in the skin of the head and face, and the other grows centralwards; on reaching the pons these bifurcate, the ascending branches arborise around the *principal sensory nucleus of the fifth* (V*d*, fig. 459), which lies just lateral to the motor nucleus, while the descending branches pass down into the bulb, where they form the descending root of the fifth, and some reach as far down in the spinal cord as the second cervical nerve. Mingled with these descending fibres are numerous nerve-cells, many of which are grouped in clusters (islands of Calleja), and the descending fibres form synapses around them. The new axons arising from the cells of the sensory nuclei pass upwards in three principal tracts:—(1) The greater number cross the raphe and join the mesial fillet; (2) some ascend the fillet of the same side; and (3) others pass into a special ascending bundle which lies near the ventricular floor (the central tract of the cranial sensory nerves).

The seventh nerve (*facial*) is the great motor nerve of the face muscles. It also supplies the platysma, the stapedius, stylo-hyoid, and posterior belly of the digastric. When it is paralysed, the muscles of the face being all powerless, the countenance acquires on the paralysed side a characteristic, vacant look, from the absence of all expression: the angle of the mouth is lower, and the paralysed half of the mouth looks longer than that on the other side; the eye has an unmeaning stare, owing to the paralysis of the orbicularis palpebrarum. All these peculiarities are exaggerated when at any time the muscles of the opposite side of the face are made active in any expression, or in any of their ordinary functions. In an attempt to blow or whistle, one side of the mouth and cheeks acts properly, but the other side is motionless, or flaps loosely at the impulse of the expired air; so, in trying to suck, one side only of the mouth acts; in feeding, the lips and cheek are powerless, and on account of paralysis of the buccinator muscle, food lodges between the cheek and gums.

The motor fibres originate from a nucleus in the ventricular floor below that of the fifth and to the outer side of that of the sixth nerve. As they curve over the nucleus of the sixth, they give off a bundle of fine fibres which cross the raphe, but their destination is unknown. The facial nucleus receives collaterals from the sensory tracts in the reticular formation.

The seventh nerve, however, is not wholly motor. The geniculate ganglion on it is of spinal type; the fibres which arise from it pass centrally into the *pars intermedia* of Wrisberg, which enters the pons between the seventh and eighth nerves; these, like other sensory fibres, divide into ascending and descending branches; the latter have been traced down to the sensory nucleus of the glosso-pharyngeal nerve. The peripheral branches of the geniculate ganglion cells pass into the large superficial petrosal and chorda tympani, the gustatory fibres of which they probably furnish. The origin of the secretory fibres of the chorda tympani is still a matter of uncertainty.

The eighth nerve (*auditory*) runs into the hinder margin of the pons by two roots. One winds round the restiform body dorsal to it, and is known as the *dorsal* or *cochlear* division; the other passes ventro-mesially on the other side of the restiform body, and is known as the *ventral* or *vestibular* division.

We will take these two parts separately. The fibres of the cochlear nerve take origin from the bipolar nerve-cells of the spiral ganglion of the cochlea; the peripheral axons ramify among the hair cells of the organ of Corti, and the central axons pass towards the pons; as they enter they bifurcate, and some pass to and arborise around a collection of nerve-cells situated between the two roots and the restiform body, called the *accessory auditory nucleus;* the remaining fibres terminate similarly in a collection of cells in the grey matter overlying the restiform body, and extending into the ventricular floor in its widest part. This is called the ganglion of the root, and the mass of grey matter is termed the *acoustic tubercle*. The auditory path is continued by new axons that arise from these cells. Those from the accessory nucleus enter the trapezium, and pass in it partly to the superior olive and trapezoid nucleus of the same side, but mainly to the corresponding nuclei of the opposite side; some fibres end here, others traverse the nuclei, and merely give off collaterals to them; they then turn upwards in the lateral fillet, and so reach the inferior C. quadrigemina. The fibres which arise in the acoustic tubercle pass superficially over the floor of the ventricle, forming the *striæ acousticæ;* having crossed the raphe, they join the fibres from the accessory nucleus in their course to the superior olive and fillet. Here again, however, a few fibres pass to the fillet of the same side.

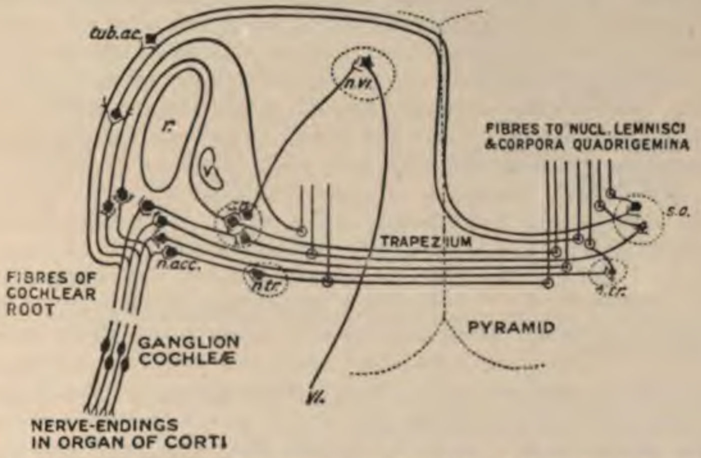

FIG. 467.—Cochlear root of the auditory nerve. *r*, restiform body; *V*, descending root of the fifth nerve; *tub. ac.*, acoustic tubercle; *n. acc.*, accessory nucleus; *s.o.*, superior olive; *n.tr.*, trapezoid nucleus; *n.VI.*, nucleus of the sixth nerve; *VI.*, issuing fibre of sixth nerve. (Schäfer.)

The vestibular nerve arises from the bipolar cells of the *ganglion of Scarpa* in the internal ear. The peripheral axons ramify among the hair cells of the epithelium in the utricle, saccule, and semicircular canals. The central axons enter a collection of small nerve-cells between the restiform body and the descending root of the fifth; this is termed the *principal nucleus;* here they bifurcate; the descending branches run towards the lower part of the bulb, and arborise around the cells of the neighbouring grey matter (descending vestibular nucleus). The ascending branches pass upwards in the restiform body to the cerebellum, in their course giving off many collaterals which form synapses with the large cells of two nuclei near the outer angle of the ventricular floor, and known as the *nucleus of Deiters* and *nucleus of Bechterew* respectively. The fibres which arise from Deiters' nucleus pass into the posterior longitudinal bundles of both sides (see p. 636); those which start in *Bechterew's nucleus* become longitudinal, but their destination is uncertain.

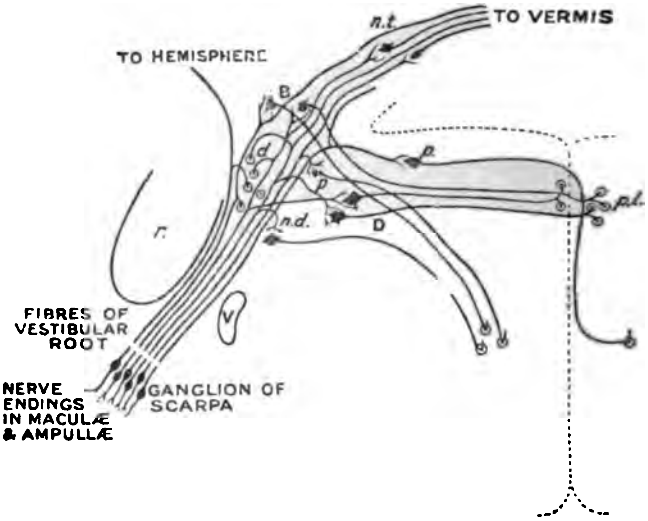

FIG. 468.—Vestibular root of the auditory nerve; *r*, restiform body; *V*, descending root of the fifth nerve; *d*, fibres of descending vestibular root; *n. d.*, cell of descending vestibular nucleus; *D*, nucleus of Deiters; B, nucleus of Bechterew: *n. t.*, nucleus tecti of cerebellum: *p. l. b.*, posterior longitudinal bundle. (Schafer.)

The accompanying diagrams (figs. 467 and 468) will serve to render these complex relationships clearer.

The ninth nerve (*glosso-pharyngeal*) gives filaments through its tympanic branch (Jacobsen's nerve) to the fenestra ovalis and fenestra rotunda, and the Eustachian tube, parts of the middle ear; also, to the carotid plexus, and through the great superficial petrosal nerve, to the spheno-palatine (Meckel's) ganglion. The small superficial petrosal (Jacobsen's nerve) passes to the otic ganglion, and thus controls the parotid secretion. The carotid plexus may also connect the nerve with the spheno-palatine ganglion. Connections are also made with the sympathetic plexus on the great meningeal artery by the external superficial petrosal. This is important, as another possible connecting link between the glosso-pharyngeal and the otic ganglion is thus provided. After communicating, either within or without the cranium, with the vagus, it leaves the cranium, divides into the two principal divisions indicated by its name, and supplies the mucous membrane of the posterior and lateral walls of the upper part of the pharynx, the Eustachian tube, the arches of the palate, the tonsils and their mucous membrane, and the tongue as far forwards as the foramen cæcum in the middle line, and to near the tip at the sides and inferior part.

It contains motor fibres to the stylo-pharyngeus, middle constrictor of pharynx, and crico-thyroid muscles, and probably to the levator palati and other muscles of the palate, except the tensor, which is supplied by the fifth nerve, and the other constrictors of the pharynx, which are supplied from the nucleus ambiguus by cranial rootlets of both ninth and tenth nerves. The nerve also contains fibres concerned in common sensation, and the sense of taste, and secretory fibres for the parotid gland. Whether the secretory fibres in the chorda tympani which pass to the submaxillary and sublingual glands originate from the seventh or ninth nerves is still uncertain.

The cells from which the motor fibres originate are situated in a special nucleus, which is a continuation upwards of the *nucleus ambiguus* (the chief motor nucleus of the tenth or vagus nerve). The sensory fibres arise in the *jugular* and *petrosal* ganglia from cells of the spinal ganglion type. When the central axons reach the bulb they bifurcate as usual; the descending branches pass down the *funiculus solitarius* and terminate in synapses around the cells scattered among its fibres. The ascending branches pass almost horizontally to arborise around the cells of the *principal nucleus* (IX in fig. 459). The arrangement, in fact, is very like that of the tenth nerve now to be described.

The tenth nerve (*vagus* or *pneumo-gastric*) has so many and important functions that I shall not attempt to describe them here; it would mean rewriting a great deal of what we have already learnt in connection with heart, respiration, digestion, etc. It is sufficient to say that it contains both efferent and afferent fibres. The efferent fibres are partly from the upper part of the combined nucleus, which lower down gives origin to the spinal accessory nerve (fig. 459, X) but mainly from the nucleus ambiguus, the position of which is shown in fig. 459, coloured blue, and also in transverse section in fig. 463. The afferent fibres originate from the cells of the ganglion of the trunk and of the root; they enter the bulb and bifurcate; the ascending branches are short and arborise around the cells of the principal nucleus (X in fig. 459); the descending fibres, together with similar ones derived from the glosso-pharyngeal nerve, pass down in the descending root of vagus and glosso-pharyngeal, which is also known as the *funiculus solitarius*. These fibres terminate by arborising around the cells of the grey matter that lies along its mesial border (*descending nucleus of vagus and glosso-pharyngeal*). This nucleus approaches the middle line as it descends, and finally joins that of the opposite side over the central canal (*commissural nucleus*).

The eleventh nerve (*spinal accessory*) is wholly efferent: it arises by two distinct origins—one from a centre in the floor of the fourth ventricle, and connected with the glosso-pharyngeal-vagus-nucleus; the other, from the outer side of the anterior cornu of the spinal cord as low down as the fourth cervical nerve. The fibres from the two origins come together at the jugular foramen, but separate again into two branches, outer and inner. The outer, consisting of large medullated fibres from the spinal origin, supplies the trapezius and sterno-mastoid muscles. The inner branch, consisting of small medullated fibres from the medulla, supplies chiefly viscero-motor filaments to the vagus. The muscles of the larynx, all of which are supplied by branches of the vagus, derive their motor nerves from the accessory; and (which is a very significant fact) Vrolik states that in the chimpanzee the internal branch of the accessory does not join the vagus at all, but goes direct to the larynx. The crico-thyroid, however, receives fibres which leave the bulb by glosso-pharyngeal rootlets; whether it receives spinal accessory fibres as well is uncertain.

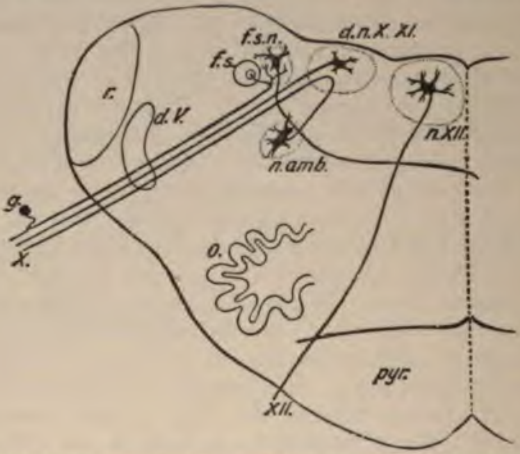

FIG. 469.—The tenth and twelfth nerves. *pyr*, pyramid; *n.XII.*, nucleus of hypoglossal; *XII.*, fibre of hypoglossal; *d.n.X.XI.*, combined nucleus of vagus and spinal accessory; *n.amb.*, nucleus ambiguus; *f.s.*, fasciculus solitarius, descending fibres of vagus and glosso-pharyngeal; *f.s.n.*, its nucleus; *X.*, motor fibre of vagus; *g*, ganglion cell in vagus trunk giving rise to a sensory fibre; *d.V.*, descending root of the fifth nerve; *r*, restiform body. (Schäfer.)

The twelfth nerve (*hypoglossal*) is also entirely efferent. It arises from a large celled and long nucleus in the bulb, close to the middle line, inside the combined nucleus of the ninth, tenth, and eleventh nerves. It receives numerous collaterals from adjacent sensory tracts, and from the descending nuclei of the fifth, ninth, and tenth nerves, and from the posterior longitudinal bundle. Fibres from this nucleus run from the ventral surface through the reticular formation in a series of bundles, and emerge from a groove between the anterior pyramid and olivary body. It is the motor nerve to the muscles of the tongue (stylo-glossus, hyo-glossus, genio-hyo-glossus, and linguales). The branches of this nerve to the genio-hyoid, thyro-hyoid, sterno-thyroid, sterno-hyoid, and omo-hyoid are branches of the first, second, and third cervical nerves carried down in its sheath and slipped off at various points as descendens (hypoglossi) cervicis.

CHAPTER XLV

STRUCTURE OF THE CEREBELLUM

THE cerebellum is composed of an elongated central portion or lobe, called the vermis or vermiform process, and two hemispheres. Each hemisphere is connected with its fellow, by means of the vermiform process.

The cerebellum is composed of white and grey matter, the latter being external, like that of the cerebrum, and like it, infolded, so that a larger area may be contained in a given space. The convolutions of the grey matter, however, are arranged after a different pattern, as shown in fig. 470. The tree-like arrangement of the white

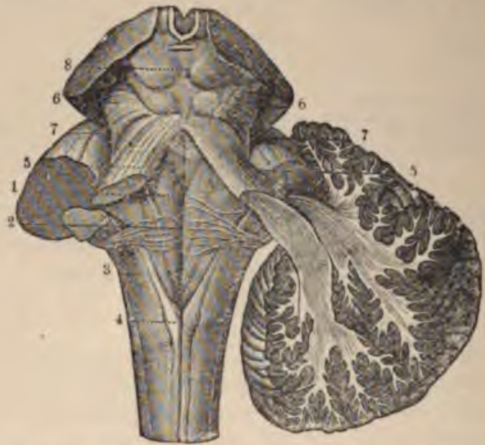

FIG. 470.—Cerebellum in section and fourth ventricle, with the neighbouring parts. 1, median groove of fourth ventricle, ending below in the *calamus scriptorius*, with the longitudinal eminences formed by the *fasciculi teretes*, one on each side; 2, the same groove, at the place where the white streaks of the auditory nerve emerge from it to cross the floor of the ventricle; 3, inferior peduncle of the cerebellum, formed by the restiform body; 4, funiculus gracilis; above this is the calamus scriptorius; 5, superior peduncle of cerebellum; 6, 6, fillet to the side of the crura cerebri; 7, 7, lateral grooves of the crura cerebri; 8, corpora quadrigemina. (From Sappey after Hirschfeld and Leveillé.)

matter has given rise to the name *arbor vitæ.* Besides the grey substance on the surface, there are, in the centre of the white substance of each hemisphere, small masses of grey matter, the largest of which, called the *corpus dentatum* (fig. 471, *cd*), resembles very closely the *corpus dentatum* of the olivary body of the medulla oblongata in appearance.

If a section is taken through the cortical portion of the cerebellum, the following distinct layers can be seen (fig. 472) by microscopic examination.

Underneath the pia mater is the *external layer* of grey matter; it is formed chiefly of fine nerve-fibres with small nerve-cells scattered through it. Into its outer part, processes of pia mater pass vertically; these convey blood-vessels. There are also here numerous long tapering neuroglia-cells. The *internal* or *granular* layer of grey matter is made up of a large number of small nerve-cells mixed with a few larger ones, and some neuroglia-cells. Between the two layers is an incomplete stratum of large flask-shaped cells, called the *cells of Purkinje.* Each of these gives off from its base a fine process which becomes the axis-cylinder of one of the medullated fibres of the white matter; the neck of the flask passing in the opposite direction breaks up into dendrites which pass into the external layer of grey matter. By Golgi's method (fig. 473) these dendrons have been shown to spread out in planes transverse to the direction of the lamellæ of the organ.

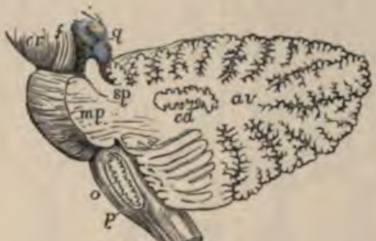

FIG. 471.—Outline sketch of a section of the cerebellum, showing the corpus dentatum. The section has been carried through the left lateral part of the pons, so as to divide the superior peduncle and pass nearly through the middle of the left cerebellar hemisphere. The olivary body has also been divided longitudinally so as to expose in section its *corpus dentatum*. *cr*, crus cerebri; *f*, fillet; *q*, corpora quadrigemina; *s p*, superior peduncle of the cerebellum divided; *m p*, middle peduncle or lateral part of the pons Varolii, with fibres passing from it into the white stem; *a v*, continuation of the white stem radiating towards the arbor vitæ of the folia; *c d*, corpus dentatum; *o*, olivary body with its corpus dentatum; *p*, pyramid. (Allen Thomson.) $\frac{2}{3}$.

Each cell of Purkinje is further invested by arborisations of two sets of nerve-fibres. One of these (originating from the fibres of the white matter which are not continuous as axis-cylinders from the cells of Purkinje) forms a basket-work round the dendrons; the other originating as axis-cylinder processes from the nerve-cells of the external layer) forms a felt work of fibrils round the body of the cell.

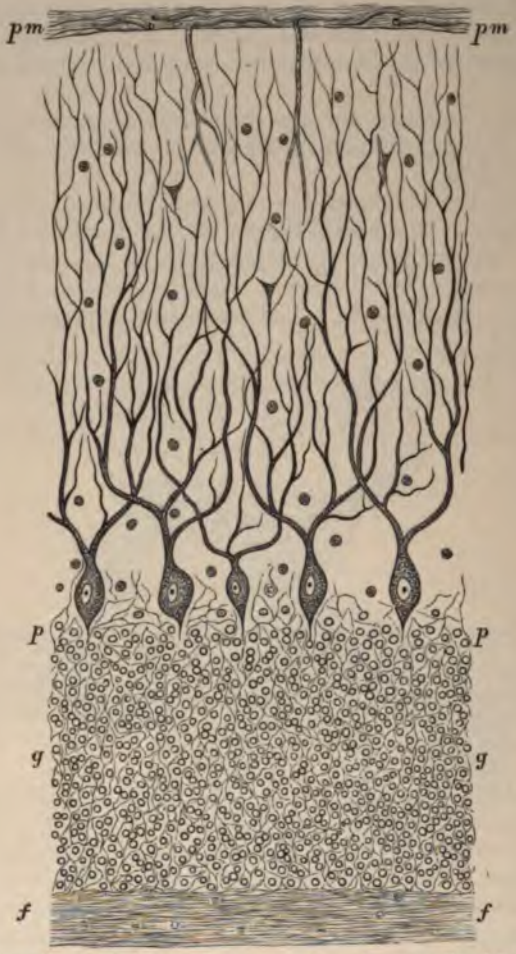

FIG. 472.—Vertical section of dog's cerebellum; *pm*, pia mater; *p*, cells of Purkinje, which are branched nerve-cells lying in a single layer and sending single processes downwards and more numerous ones upwards, which branch continuously and extend through the external "molecular layer" towards the free surface; *g*, dense (granular) layer of small nerve-cells; *f*, layer of nerve-fibres, with a few scattered nerve-cells. This last layer (*f f*) constitutes part of the *white* matter of the cerebellum, while the layers between it and the free surface are *grey* matter. (Klein and Noble Smith.)

The cells of the internal layer of grey matter are small; their dendrites intermingle with those of neighbouring cells; their axons penetrate into the external layer, but their final destination is uncertain. Ramifying among these cells are fibres characterised by possessing bunches of short branches at intervals (moss-fibres of Cajal).

The peduncles of the cerebellum are three in number—superior, middle, and inferior; we have already had occasion to mention them in our study of the bulb, pons, and mid-brain. The course of the fibres has been studied by the degeneration method. The *superior* peduncle consists mainly of fibres which originate in the corpus dentatum; some fibres are said to arise in the cerebellar hemisphere, and to pass through the corpus dentatum without communicating with its cells. These fibres cross the raphe in the mid-brain, and terminate in the red or tegmental nucleus. The direction of the impulses in these fibres is from cerebellum to cerebrum, the red nucleus being a cell station on the road. There appear, however, to be some fibres starting from the optic thalamus which convey impulses in the opposite direction. In addition to these there is Cajal's *descending cerebellar bundle.*

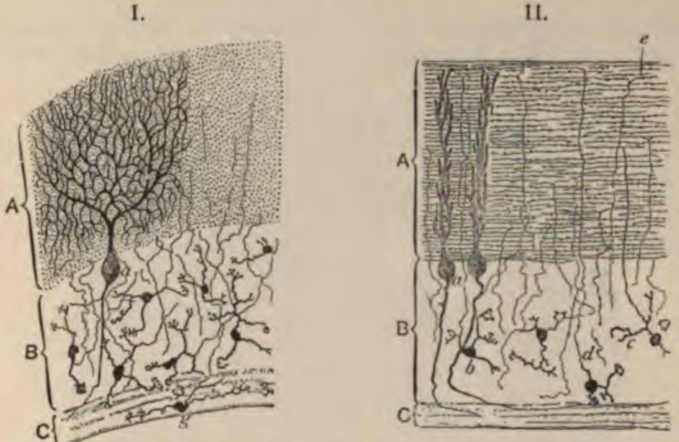

FIG. 473.—Section of cerebellar cortex, stained by Golgi's method; I. taken across the lamina; II. in the direction of the lamina; A, outer or molecular layer; B, inner or granular layer; C, white matter. *a*, Cell of Purkinje; *b*, small cells of inner layer; *c*, dendrons of these cells; *d*, axis-cylinder process of one of these cells becoming longitudinal in the outer layer; *e*, bifurcation of one of these; *g*, a similar cell lying in the white matter. (Ramon y Cajal.)

This consists of branches which are given off by the fibres before they cross at the raphe; they pass towards the bulb, giving off collaterals to the motor nucleus of the fifth nerve, to the facial nucleus, to the nucleus ambiguus, and others. One must not forget that besides all these fibres that the tract of Gowers joins the superior peduncle, and runs back along its mesial border to the vermis.

The *middle* peduncle consists of fibres which form the anterior transverse fibres of the pons. They pass from the nuclei pontis to the opposite cerebellar hemisphere. Others convey impulses in the opposite direction from the hemisphere to the pons; on section, these fibres degenerate as far as the raphe, where they intermingle with those from the opposite side.

The *inferior* peduncle or restiform body is composed of ascending fibres, which pass into it from the direct cerebellar tract, from both olivary nuclei, but mainly from that of the opposite side, from the nucleus gracilis and nucleus cuneatus, and from the nuclei of the sensory roots of the cranial nerves. The fibres pass mostly to the vermis, crossing to the opposite side over the fourth ventricle, but giving off strong collaterals to the cerebellar hemisphere of the same side; these account for the fact that each cerebellar hemisphere is in principal physiological connection with the same side of the spinal cord.

CHAPTER XLVI

STRUCTURE OF THE CEREBRUM

THE cerebrum consists of two halves called *cerebral hemispheres,* separated by a deep longitudinal fissure and connected by a large band of transverse commissural fibres known as the *corpus callosum* (fig. 474). The interior of each hemisphere contains a cavity of com-

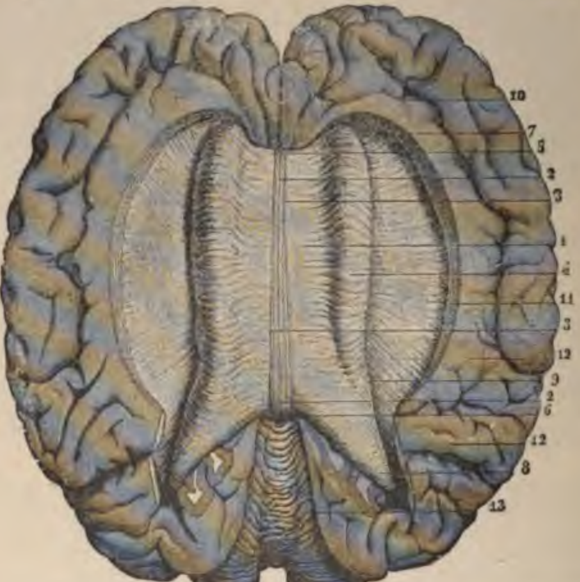

FIG. 474.—View of the Corpus Callosum from above. $\frac{1}{2}$.—The upper surface of the corpus callosum has been fully exposed by separating the cerebral hemispheres and throwing them to the side; the gyrus fornicatus has been detached, and the transverse fibres of the corpus callosum traced for some distance into the cerebral medullary substance. 1, the upper surface of the corpus callosum; 2, median furrow or raphe; 3, longitudinal striæ bounding the furrow; 4, swelling formed by the transverse bands as they pass into the cerebrum; 5, anterior extremity or knee of the corpus callosum; 6, posterior extremity; 7, anterior, and 8, posterior part of the mass of fibres proceeding from the corpus callosum; 9, margin of the swelling; 10, anterior part of the convolution of the corpus callosum; 11, hem or band of union of this convolution; 12, internal convolutions of the parietal lobe; 13, upper surface of the cerebellum. (Sappey after Foville.)

plicated shape called the *lateral ventricle;* the lateral ventricles open into the third ventricle. Fig. 475 represents a dissected brain in which the corpus callosum has been removed; the ventricles are thus exposed.

Each hemisphere is covered with grey matter, which passes down into the fissures. This surface grey matter is called the *cerebral cortex.* The amount of this grey matter varies directly with the amount of convolution of the surface. Under it white matter is situated; and at the base there are masses of grey matter; part of these *basal ganglia* are seen forming part of the wall of the ventricles. The anterior basal ganglion is called the *corpus striatum;* it is

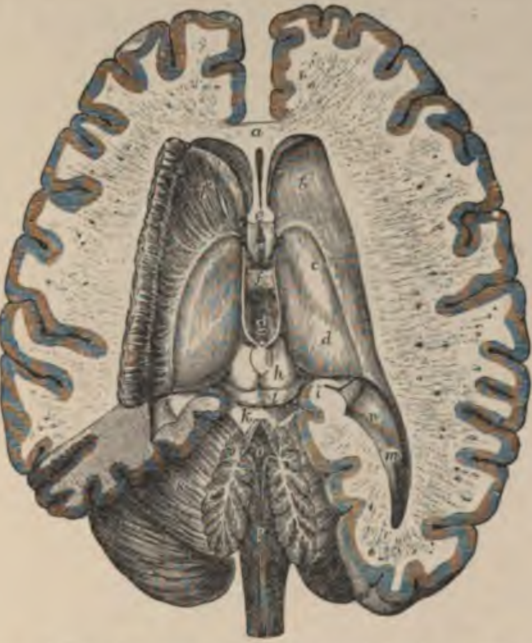

FIG. 475.—Dissection of brain, from above, exposing the lateral, fourth, and fifth ventricles with the surrounding parts. $\frac{1}{2}$.—*a*, anterior part, or *genu* of corpus callosum; *b*, corpus striatum; *b′*, the corpus striatum of left side, dissected so as to expose its grey substance; *c*, points by a line to the tænia semicircularis; *d*, optic thalamus; *e*, anterior pillars of fornix divided; below they are seen descending in front of the third ventricle, and between them is seen part of the anterior commissure; in front of the letter *e* is seen the slit-like fifth ventricle, between the two laminæ of the septum lucidum; *f*, soft or middle commissure; *g* is placed in the posterior part of the third ventricle; immediately behind the latter are the posterior commissure (just visible) and the pineal gland, the two crura of which extend forwards along the inner and upper margins of the optic thalami; *h* and *i*, the corpora quadrigemina; *k*, superior crus of cerebellum; close to *k* is the valve of Vieussens, which has been divided so as to expose the fourth ventricle; *l*, hippocampus major and corpus fimbriatum, or tænia hippocampi; *m*, hippocampus minor; *n*, eminentia collateralis; *o*, fourth ventricle; *p*, posterior surface of medulla oblongata; *r*, section of cerebellum; *s*, upper part of left hemisphere of cerebellum exposed by the removal of part of the posterior cerebral lobe. (Hirschfeld and Leveillé.)

divided into two parts called the *lenticular* or *extraventricular nucleus,* and the *caudate* or *intraventricular nucleus.* It has received the latter name because it is seen in the interior of the ventricle. The posterior basal ganglion is called the *optic thalamus.*

Passing up between the basal ganglia are the white fibres which enter the cerebral hemisphere from the crus; these constitute the *internal capsule.* This passes in front between the two subdivisions of the corpus striatum, and behind between the optic thalamus and the lenticular nucleus of the corpus striatum.

The relationship of these parts is best seen in a vertical section; such as is represented in the next diagram (fig. 476).

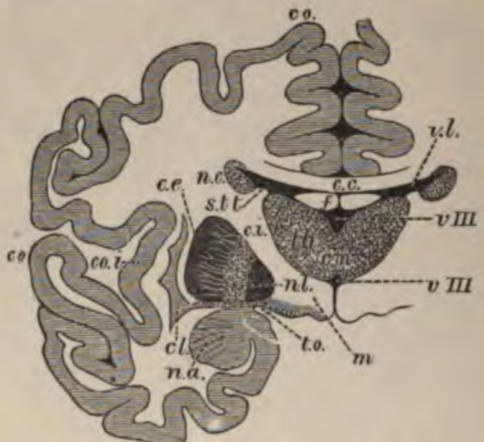

FIG. 476.—Vertical section through the cerebrum and basal ganglia to show the relations of the latter. *co.*, cerebral convolutions; *c.c.*, corpus callosum; *v.l.*, lateral ventricle; *f*, fornix; *vIII.*, third ventricle; *n.c.*, caudate nucleus; *th*, optic thalamus; *n.l.*, lenticular nucleus; *c.i.*, internal capsule; *cl.*, claustrum; *c.e.*, external capsule; *m*, corpus mammillare; *t.o.*, optic tract; *s.t.t.*, stria terminalis; *n.a.*, nucleus amygdalæ; *cm*, soft commissure; *co.i.*, Island of Reil. (Schwalbe.)

One hemisphere is seen, with portions of the other. The surface darkly shaded indicates the grey matter of the cortex, which passes down into the fissures; one very extensive set of convolutions (*co.i.*), passes deeply into the substance of the hemisphere; this is called the Island of Reil; the lowest stratum of grey matter is separated from this to form a narrow isolated strip of grey matter called the *claustrum* (*cl.*). In the middle line from above down are seen the great longitudinal fissure extending as far as (*c.c.*) the corpus callosum, the band of white matter that forms the great commissure between the two hemispheres; beneath this are the lateral ventricles which communicate by the *foramen of Munro* with the third ventricle: *the fornix* is indicated by the letter *f.* Contributing to the floor of the lateral ventricle, one next sees the optic thalamus (*th.*), and the tail end of the nucleus caudatus (*n.c.*); the section being taken somewhat posteriorly. The nucleus lenticularis is marked *nl.*; and the band of white fibres passing up between it and the thalamus is called the *internal capsule* (*c.i.*); the narrow piece of white matter between the claustrum and the lenticular nucleus is called the *external capsule*.

For the student of medicine the internal capsule is one of the most important parts of the brain. Into it are continued up the fibres which we have previously traced as far as the crus cerebri; the motor-fibres of the crusta are continued into the anterior two-thirds of its posterior limb (*i.e.* behind the genu * in fig. 477); the sensory fibres of the tegmentum into the posterior third of this limb. When these fibres get beyond the narrow pass between the basal ganglia, they spread out in a fan-like manner and are distributed to the grey cortex; the motor-fibres coming down from the motor convolutions around the fissure of Rolando; the sensory fibres going to the same convolutions and also to others behind these which are associated with special sensations. The name *corona radiata* is applied to the fan-like spreading of the fibres; the fibres as they pass through the handle of the fan, or internal capsule, communicate with the nerve-cells of the grey matter of the basal ganglia; the pyramidal fibres on their way down to the medulla and cord from the motor areas of the brain send off collaterals or side branches which arborise around the cells of the corpus striatum, and to a lesser degree around those of the optic thalamus; the axis-cylinder processes of these cells pass out to join the pyramidal tract on its downward course. The sensory fibres on their way up may pass straight on to the cortex, but the majority, especially those in the fillet, terminate by arborising round the cells of the optic thalamus, and in the *subthalamic area*. This, in fact, is another cell-station or position of relay: the fibres passing out from the cells of the thalamus continue the impulse on to the cortex.

The importance of the internal capsule is rendered evident when one considers the blood supply of these parts; at the *anterior and posterior perforated spots*, numerous small blood-vessels enter for the supply of the basal ganglia, and these are liable to become diseased, and if they rupture, a condition called *apoplexy* is the result; if the hæmorrhage is excessive, death may occur almost immediately; but if the patient recovers, a condition of more or less permanent paralysis remains behind; and a very large amount of paralysis results from a comparatively limited lesion, because so many fibres are congregated together in this narrow isthmus of white matter. If the hæmorrhage is in the anterior part of the posterior limb, motor paralysis of the opposite side of the body (hemiplegia) will be the most marked symptom. If the hæmorrhage occurs in the posterior part, sensory paralysis of the opposite side of the body will be the most marked symptom. If the motor-fibres are affected, degeneration will occur in the pyramidal tract, and can be traced through the pes of the crus and mid-brain to the pyramid of the pons and bulb, and then in the crossed pyramidal tract of the opposite side and in the direct pyramidal tract of the same side of the cord.

Fig. 477 represents a horizontal view through the hemisphere. The internal capsule (*c*) at the point * makes a bend called the *genu* or knee, behind which the motor-fibres, and more posteriorly still sensory-fibres, pass. The connection between cerebrum and the cerebellum is also indicated; one cerebral hemisphere is connected with the opposite cerebellar hemisphere by fronto-cerebellar and temporo-occipito-cerebellar fibres which pass respectively in front of and behind the pyramidal fibres in the internal capsule.

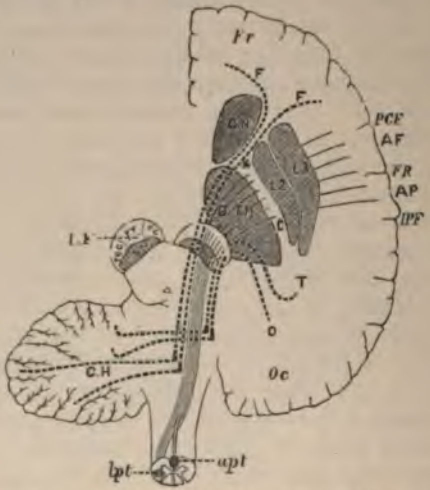

FIG. 477.—Diagram to show the connection of the Frontal and Occipital Lobes with the Cerebellum, etc. The dotted lines passing in the crusta (T.OC), outside the motor fibres, indicate the connection between the temporo-occipital lobe and the cerebellum. F.C., the fronto-cerebellar fibres, which pass anteriorly to the motor tract in the crusta; L.F., fibres from the caudate nucleus to the pons. *Fr.*, frontal lobe; *Oc.*, occipital lobe; AF., ascending frontal; AP., ascending parietal convolutions; PCF., precentral fissure in front of the ascending frontal convolution; FR., fissure of Rolando; IPF., intraparietal fissure. A section of the crus is lettered on the left side. S.N., substantia nigra; PY., pyramidal motor fibres, which on the right are shown as continuous lines converging to pass through the posterior limb of I.C., internal capsule (the knee or elbow of which is shown thus *) upwards into the hemisphere and downwards through the pons to cross at the medulla in the pyramidal decussation. *lpt*, crossed pyramidal tract; *apt*, direct pyramidal tract. (Gowers.)

Histological Structure of the Cerebral Cortex.

The grey matter of the cortex is composed of a number of layers which are, however, not well marked off from one another. The number of these layers is variously given by different authorities from three up to nine. The most satisfactory division appears to me to be that into three.

1. *The molecular layer.*—Most superficially is a thin stratum of medullated nerve-fibres largely derived from the dendrons of the cells of the next layer. The nerve-cells (F in fig. 479) intermingled with these are branched, and have several processes which lie horizontally beneath the surface (tangential fibres). Neuroglia cells are also present.

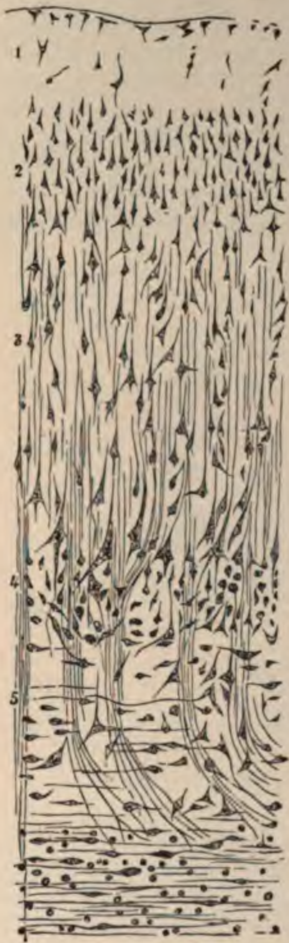

FIG. 478.—The layers of the cortical grey matter of the cerebrum. (Meynert.)

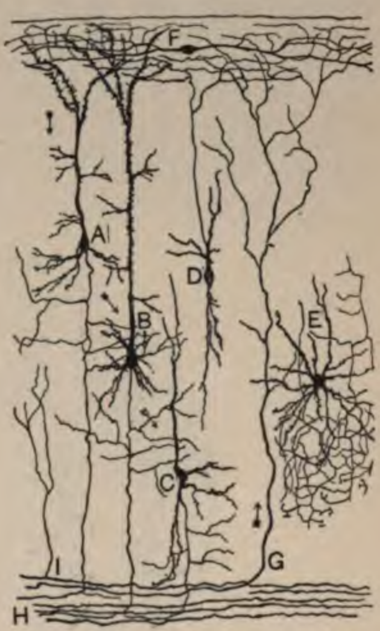

FIG. 479.—Principal types of cells in the cerebral cortex.

A, medium-sized pyramidal cell of the second layer.
B, large pyramidal cell.
C, polymorphous cell.
D, cell of which the axis-cylinder process is ascending.
E, neuroglia cell.
F, cell of the first, or molecular, layer, forming an intermediate cell-station between sensory fibres and motor cells. Notice the *tangential* direction of the nerve-fibres.
G, sensory fibre from the white matter.
H, white matter.
I, collateral of the white matter. (Ramon y Cajal.)

2. *The layer of pyramids.*—There are several deep, and the largest cells are situated most deeply. Each of these has an apical process running to the surface, where the branches run tangentially. The lateral processes are also branched dendrons. The axon originates from the base. The largest pyramids (Betz cells) are found in the so-called motor cortex (Rolandic area) and give origin to the fibres of the pyramidal tract. The smaller pyramids are association units.

3. *The layer of polymorphous cells.*—There are small scattered cells, many of a fusiform shape. In the Island of Reil this layer is hypertrophied, and is separated from the rest of the grey matter by a stratum of white fibres; it is known then as the *claustrum*.

Variations in different regions of the cortex will be found described in histological works, but the physiological meaning of these is not clear in many cases. The Golgi method has proved conspicuously useful in the study of the shapes and dispositions of the cells (see figs. 479, 480, 481). Bundles of medullated nerve-fibres pass in vertical streaks through the deeper layers of the grey matter; some of these are axis cylinder processes of the pyramidal and polymorphous cells, and are conveying impulses downwards; others conveying impulses upwards pass from the white matter into the cortex to arborise among its various cells. In addition to these fibres, other strands lie parallel to the surface of the cortex, and have received various names, such as the outer line of Baillarger in the layer of medium-sized pyramids, the inner line of Baillarger in the layer of large pyramids, and the

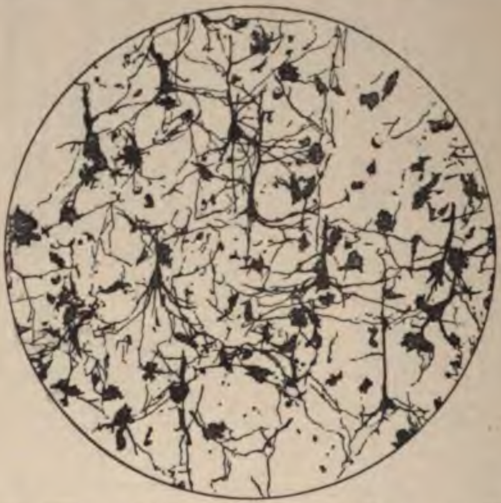

FIG. 480.—Human cerebral cortex: Golgi's method. Low power. (Mott.)

line of Gennari in the occipital region. There can be little or no doubt that these are association tracts linking the convolutions together.

The cells of the cortex thus give rise to the motor or efferent fibres; these pass into the white matter of the interior of the brain. Some go either directly or by collaterals, (1) to the cortex of more or less distant convolutions. These are called *Association fibres.* (2) Others pass to the corpus callosum, and so reach the cortex of the opposite hemisphere. These are called *Commissural fibres.* In each case they terminate by arborisations (synapses) around the cells of the grey matter of the cortex; while others again, especially those of the largest pyramidal cells, extend downward through the corona radiata and internal capsule, and become, (3) fibres of the pyramidal tract. These are called *Projection fibres.* As they pass down they give off collaterals to the adjacent grey matter, to the opposite hemisphere *viâ* the corpus callosum, to the corpus striatum and the optic thalamus, which terminate there by arborisations; the main fibres terminate in synapses round the multipolar cells of the grey matter of the opposite side of the spinal cord. These are termed the cortico-spinal fibres; von Monakow has shown that some of the pyramidal fibres terminate in the mid-brain and pons (cortico-pontine fibres), and a fresh relay of fibres thence continues the impulse downwards.

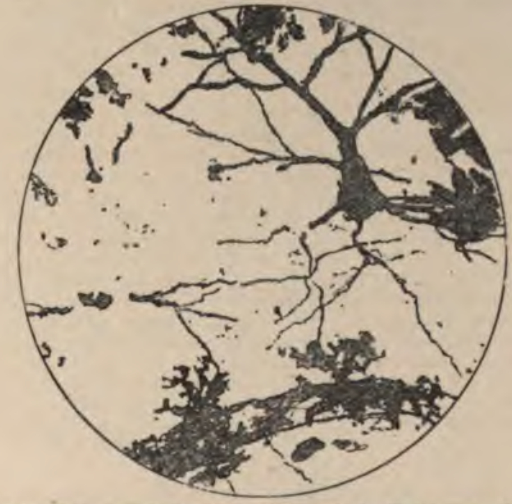

FIG. 481.—Human cerebral cortex: Golgi's method. High power. (Mott.)

The cells of the cortex are, in addition to all this, surrounded by the arborising terminations of the sensory nerve-fibres, which, after relays at various cell-stations, ultimately reach the cortex.

We are now in a position to complete diagram 448 (p. 613), and obtain an idea of the relations of the principal cells and fibres of the cerebro-spinal nervous system to one another.

Pyr. (fig. 482) is a cell of the Rolandic area of the cerebral cortex; AX is its axis-cylinder process which passes down in the pyramidal tract, and crosses the middle line AB at the pyramidal decussation. It gives off collaterals, one of which (*call*) is shown passing in the corpus callosum to terminate in an arborisation in the cortex of the opposite hemisphere; another (*str*) passes into the corpus striatum. In the cord collaterals pass off and end in arborisations round cells of the anterior horn of the spinal cord (see also fig. 448); the main fibre has a similar termination.*

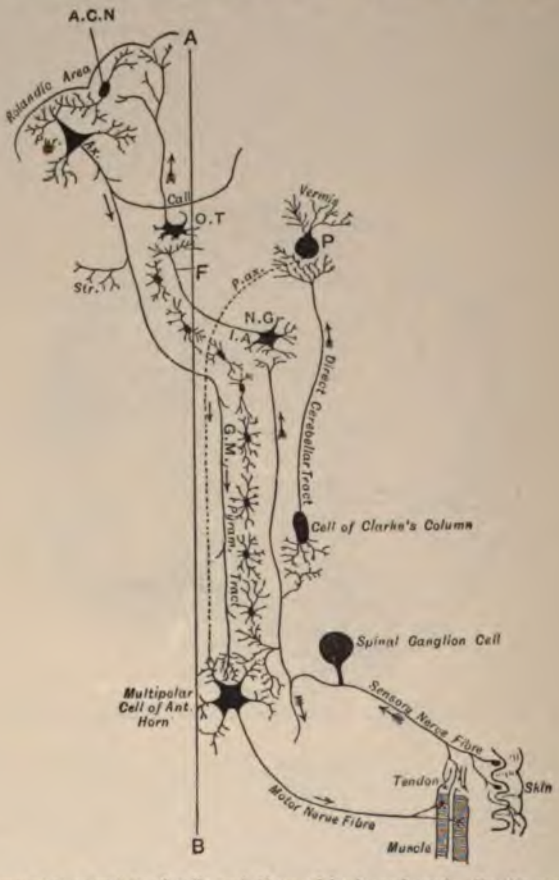

FIG. 482.—Scheme of relationship of cells and fibres of brain and cord. (In the preparation of this diagram I have received considerable assistance from Dr Mott.)

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* The intermediate cell station in the posterior horn between the pyramidal fibre and the anterior cornual cell (Schäfer) is not shown in the diagram (see also p. 613).

The motor nerve-fibre passes from the anterior cornual cell to muscular fibres, where it ends in the terminal arborisations called end-plates.

Coming now to the sensory fibres, a cell of one of the spinal ganglia is shown. Its axis-cylinder process bifurcates, and one branch passes to the periphery, ending in arborisations in skin and tendon. The other (central) branch bifurcates on entering the cord, and its divisions pass upwards and downwards, the latter for a short distance only; the terminations of this descending branch and of collaterals of the ascending branch round the cells of the spinal cord are more fully shown in fig. 448. The main ascending branch arborises around a cell of the nucleus gracilis (N.G.) or nucleus cuneatus in the posterior columns of the bulb; the axis-cylinder process of this cell passes over to the other side as an internal arcuate fibre (I.A.), and becomes longitudinal as one of the fibres of the mesial fillet (F), which terminates round a cell of the optic thalamus (O.T.), from which a new axis-cylinder process passes to form an arborisation around the dendrons of one of the cerebral cells (Cajal's nerve-unit of association A.C.N.) in the surface layer of the cortical grey matter (shown on a larger scale in fig. 479 F); the axis-cylinder process of A.C.N. arborises round the dendrons of the pyramidal cell from which we started.

In this way one gets a complete physiological circle of nerve-units; the segments of the circle are, however, anatomically distinct, and the impulses travel through contiguous, not through continuous, structures. The simple arrows indicate the direction of the impulses in the efferent projection system; the feathered arrows in the afferent projection system.

Next we come to the connections of the cerebellum. One of the collaterals of the sensory nerve-fibre arborises round a cell of Clarke's column, from which a fibre of the direct cerebellar tract passes to end in an arborisation around a cell in the vermis of the cerebellum. P is one of the cells of Purkinje, the axis-cylinder process of which P.ax passes to the cerebro-spinal axis; it is depicted as passing down to envelop one of the cells of the anterior horn; but this has never been satisfactorily demonstrated; so a dotted line has been used to indicate this uncertainty. No doubt also some of its collaterals pass up to the cerebrum.

The origin and destination of the tract of Gowers are not shown in the diagram; the fibres of communication from the cerebral to the opposite cerebellar hemisphere, which pass through the superior cerebellar peduncle, are also omitted. The sympathetic system, with its numerous cell stations in the sympathetic ganglia, we have studied in connection with the blood-vessels and viscera to which the sympathetic fibres are distributed (see especially pp. 299-303).

G.M. is the grey matter which is continuous from spinal cord to the optic thalamus, and through this certain afferent impulses, such as those of pain, travel upwards.

Particular attention should be paid to the following point: when an afferent fibre enters the spinal cord, it divides into three main sets of branches. The first set, the shortest, forms synapses with the motor cells of the anterior horn; here we have the anatomical basis of spinal reflex action. The second set passes through an intermediate cell-station in Clarke's column to the cerebellum, the emerging fibres from which also influence the motor discharge of the anterior horn cells. The third set, the longest, passes through three intermediate cell-stations (the first in the nucleus gracilis or cuneatus, the second in the optic thalamus, the third in the association units in the cortex), and ultimately reaches the pyramidal nerve-cells of the cerebral cortex, the efferent fibres (pyramidal fibres) of which pass to the motor cells of the anterior cornu and influence their discharge. The motor nerve-cells of the anterior horn may thus be influenced by the afferent impulses *viâ* three paths or *nervous circles.* In health, all these nervous circles are in action to produce co-ordinated muscular impulses. In locomotor ataxy, which is a degeneration of the cells of the ganglia on the posterior roots and their branches, all these nervous circles are deranged, and the result is loss of reflex action, and inco-ordination of muscular movements.

It should be noted that the pyramidal cells in the cortex, though the largest in size, are the least numerous. Similarly the large motor cells of the cord are relatively few in number. The innumerable smaller cells in both situations are association cells concerned in the co-ordination of impulses.

The Convolutions of the Cerebrum.

The surface of the brain is marked by a great number of depressions which are called *fissures* or *sulci*, and it is this folding of the surface that enables a very large amount of the precious material called the grey matter of the cortex to be packed within the narrow compass of the cranium. In the lowest vertebrates the surface of the brain is smooth, but going higher in the animal scale the fissures make their appearance, reaching their greatest degree of complexity in the higher apes and in man.

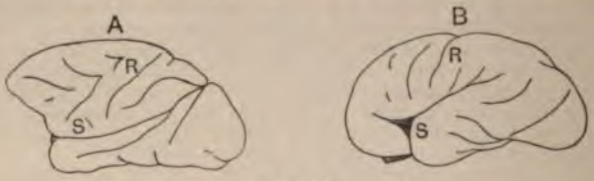

FIG. 483.

A. Cerebral Hemisphere of adult Macacque monkey.
B. Cerebral Hemisphere of child shortly before birth.

The two brains are very much alike, but the growth forwards of the frontal lobes even at this early stage of development of the human brain is quite well seen. S, fissure of Sylvius; R, fissure of Rolando.

In an early embryonic stage of the human fœtus the brain is also smooth, but as development progresses the sulci appear, until the climax is reached in the brain of the adult.

The sulci, which make their appearance first, both in the animal scale and in the development of the human fœtus, are the same. They remain in the adult as the deepest and best marked sulci; they are called the *primary fissures* or *sulci*, and they divide the brain into *lobes;* the remaining sulci, called the *secondary fissures* or *sulci*, further subdivide each lobe into *convolutions* or *gyri*.

A first glance at an adult human brain reveals what appears to be a hopeless puzzle; this, however, is reduced to order when one studies the brain in different stages of development, or compares the brain of man with that of the lower animals. The monkey's brain in particular has given the key to the puzzle, because there the primary fissures are not obscured by the complexity and contorted arrangement of secondary fissures.

The preceding figure, comparing the brain of one of the lower monkeys with that of the child shortly before birth, shows the close family likeness in the two cases.

Fig. 484 gives a representation of the brain of one of the higher monkeys, the orang-outang, where there is an intermediate condition of complexity by which we are led lastly to the human brain.

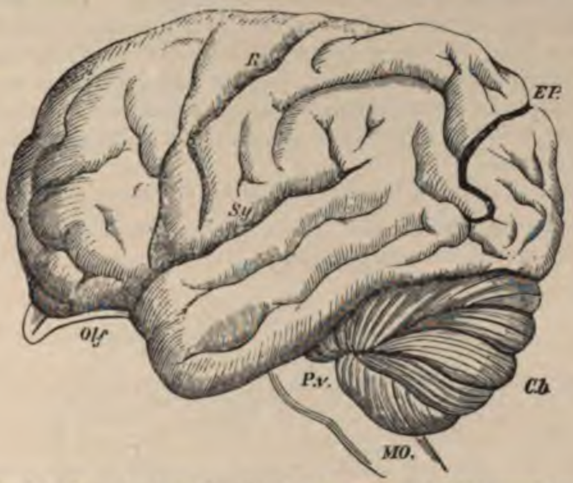

FIG. 484.—Brain of the Orang, ⅔ natural size, showing the arrangement of the convolutions *Sy*, fissure of Sylvius; *R*, fissure of Rolando; *EP*, external parieto-occipital fissure; *Olf*, olfactory lobe; *Cb*, cerebellum; *PV*, pons Varolii; *MO*, medulla oblongata. As contrasted with the human brain, the frontal lobe is short and small relatively, the fissure of Sylvius is oblique, the temporo-sphenoidal lobe very prominent, and the external parieto-occipital fissure very well marked. Note also the bend or genu in the Rolandic fissure. This is found in all anthropoid apes.

Let us take first the outer surface of the human hemisphere; the primary fissures are—

1. *The fissure of Sylvius;* this divides into two limbs, the posterior of which is the larger, and runs backwards and upwards, and the anterior limb, which, passing into the substance of the hemisphere, forms the *Island of Reil.*

2. *The fissure of Rolando,* running from about the middle of the top of the diagram (fig. 485) downwards and forwards.

3. *The external parieto-occipital fissure* (PAR. OC. F) parallel to the fissure of Rolando but more posterior and much shorter; in monkeys it is longer (see fig. 484).

These three fissures divide the brain into five lobes:—

1. *The frontal lobe;* in front of the fissure of Rolando.

2. *The parietal lobe;* between the fissure of Rolando and the external parieto-occipital fissure.

3. *The occipital lobe;* behind the external parieto-occipital fissure.

4. *The temporo-sphenoidal lobe;* below the fissure of Sylvius.

5. *The Island of Reil.*

It will be noticed that the names of the lobes correspond to those of the bones of the cranial vault which cover them. There is no exact correspondence between the bones and the lobes, but the precise position of the various convolutions in relation to the surface of the skull is a matter of anatomy, which, in these days of brain-surgery, is of overwhelming importance to the surgeon. The position of a localised disease in the brain can be determined very accurately, as we shall see later, by the symptoms exhibited by the patient, and it would be obviously inconvenient to the patient if the surgeon was unable to trephine over the exact spot under which the diseased convolution lies, but had to make a number of exploratory holes to find out where he was.

Each lobe is divided into convolutions by secondary fissures.

1. **The frontal lobe** is divided by the *central frontal* or *prefrontal sulcus,* which runs upwards parallel to the fissure of Rolando, and two *transverse frontal sulci,* upper and lower, into four convolutions; namely, the *ascending frontal convolution* in front of the fissure of Rolando, and three *transverse frontal convolutions, upper, middle, and lower,* which run outwards and forwards from it.

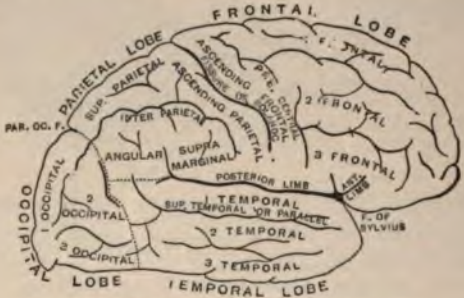

FIG. 485.—Right cerebral hemisphere, outer surface.

2. **The parietal lobe** has one important secondary sulcus, at first running parallel to the fissure of Rolando and then turning back parallel to the margin of the brain. It is called the *intra-parietal sulcus.* The lobe is thus divided into the *ascending parietal convolution* behind the fissure of Rolando, the *supra-marginal convolution* between the intra-parietal sulcus, and the fissure of Sylvius; the *angular convolution* which turns round the end of the Sylvian fissure,

and the *superior parietal convolution*, or *parietal lobule*, in front of the external parieto-occipital fissure.

3. **The occipital lobe** is divided into *upper, middle, and lower occipital convolutions* by two secondary fissures running across it.

4. **The temporal or temporo-sphenoidal lobe** is similarly divided into *upper, middle, and lower temporal convolutions* by two fissures running parallel to the fissure of Sylvius; the upper of these fissures is called the *parallel fissure*.

5. **The Island of Reil** is divided into convolutions by the breaking up of the anterior limb of the Sylvian fissure.

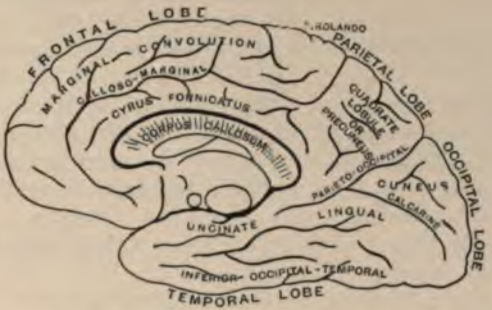

FIG. 486.—Right cerebral hemisphere, mesial surface.

Coming now to the mesial surface of the hemisphere (fig. 486), its subdivisions are made evident by cutting through the corpus callosum which unites the hemisphere to its fellow. The subdivision into lobes is not so apparent here as on the external surface of the hemisphere, so we may pass at once to the convolutions into which it is broken up by fissures.

In the middle the corpus callosum is seen cut across; above it and parallel to its upper border is a fissure called the *calloso-marginal fissure* which turns up and ends on the surface near the upper end of the fissure of Rolando. The convolution above this is called the *marginal convolution*, and the one below it the *callosal convolution* or *gyrus fornicatus*. The deep fissure below the corpus callosum running from its posterior end forwards and downwards is called the *dentate fissure;* this forms a projection seen in the interior of the lateral ventricle, and called there the *hippocampus major;* it is sometimes called the *hippocampal convolution* which, together with the gyrus fornicatus above the corpus callosum, constitutes the *limbic lobe*. Below the dentate fissure is another called the *collateral fissure*, above which is the *uncinate convolution*, and below which is the inferior temporal convolution which we have previously seen on the external surface of the hemisphere (see fig. 485). In the occipital region the internal *parieto-occipital fissure*, which is a continuation of the external parieto-occipital fissure, passes downwards and forwards till it meets the *calcarine fissure;* these two enclose between them a wedge-shaped piece of brain called the *cuneus* or *cuneate lobule;* the square piece above it is called the *precuneus* or *quadrilateral lobule.*

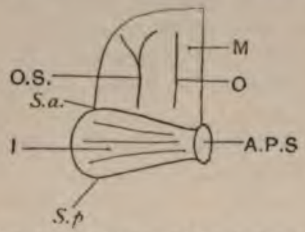

FIG. 487.—Orbital surface of frontal lobe.

M, marginal convolution.
O, olfactory sulcus.
O.S., orbital sulcus.
I, island of Reil.
S.a., anterior limb of Sylvian fissure.
S.p., posterior limb of Sylvian fissure.
A.P.S., anterior perforated spot.

The only convolutions now left are those which are placed on the surface of the frontal lobe that rests on the orbital plate of the frontal bone; they are shown in fig. 453, 2 2′ 2″ (p. 622), and may be seen diagrammatically in fig. 487, the end of the temporal lobe being cut off to expose the convolutions of the central lobe or Island of Reil.

Along the edge is the continuation of the marginal convolution (M); next comes the olfactory sulcus (O) in which the olfactory tract and bulb lie; then the triradiate *orbital sulcus* (O.S.) which divides the rest of this surface into three convolutions.

CHAPTER XLVII

FUNCTIONS OF THE SPINAL CORD

THE functions of the spinal cord fall into two categories: functions of the grey matter, which consist in the reflection of afferent impulses, and their conversion into efferent impulses (*reflex action*); and functions of the white matter, which are those of *conduction*.

The Cord as an Organ of Conduction.

We have studied at some length the various paths in the white matter, and so we have the materials at hand for recapitulating the main facts in connection with the physiological aspect of the problem.

Complete section of the spinal cord in animals, and diseases or injuries of the cord or spinal canal in man, which practically cut the cord in two, lead to certain *histological* changes of a degenerative nature, which we have already studied, and to *physiological* results, which are briefly—(1) paralysis, both motor and sensory, of the parts of the body supplied by spinal nerves which originate below the point of injury; and (2) increased reflex irritability of the same parts, the reason for which we shall study immediately.

Hemisection of the cord leads to degenerative changes on the same side of the cord, and loss of motion and sensation on the same side of the body below the lesion (see p. 619).

The main motor path in the cord from the brain is the pyramidal tract; the anatomy of this tract is described in Chapters XLII. to XLVI., and we need do no more here than remind the reader that it originates from the pyramidal cells of the cortex of the opposite cerebral hemisphere, and that the principal decussation occurs at the lower part of the bulb.

The sensory tracts are more complex, on account of the numerous cell-stations on their course. The path for tactile and muscular sense impressions is up the posterior columns to the nucleus gracilis and nucleus cuneatus; thence by the internal arcuate fibres and fillet to the optic thalamus of the opposite side, and thence by the posterior part of the internal capsule to the Rolandic area of the hemisphere; the decussation of the fillet occurs in the bulb.

Schiff, one of the earliest to work at the subject of conducting paths in the cord, arrived at the conclusion that painful impressions travelled to the brain by the grey matter of the cord. This conclusion was regarded as paradoxical, for white matter is conducting, grey matter is central or reflecting. But the conclusion is not so paradoxical as it appears at first sight, for we now know the grey matter is made up of nerve-units, communicating physiologically by their interlacement of dendrons; and it is quite easy to understand that impulses may travel up grey matter through a vast series of cell stations or positions of relay. The more exact methods of modern research have gone far to justify Schiff's conclusions, and it is now generally held that the impulses due to painful impressions, and also those produced by heat and cold, travel up to the optic thalamus by the loopings of fibres from cell to cell through the tract of grey matter, which is continuous from cord to optic thalamus (fig. 482, G.M.); from the optic thalamus the fibres of the corona radiata carry on the impulse to the cortex. These conclusions are confirmed by recent experiments on hemisection (see p. 619), and by the phenomena seen in certain diseases. One of the most instructive of these from the physiological standpoint is known as *locomotor ataxy*. This disease is an affection of the afferent neurons, and the most marked and constant change in the spinal cord is a degenerative one in the posterior columns. In such a case muscular and tactile sense are abolished, particularly in the lower limbs, but painful and thermal sensations are felt. On the other hand, in the disease of the grey matter of the cord called *syringomyelia*, sensations of heat, cold, and pain are lost, and tactile sensations remain.

Some afferent impulses reach the cerebellum *viâ* the cells of Clarke's column and the direct or dorsal cerebellar tract to the restiform body and inferior peduncle of the cerebellum. It terminates in the vermis or middle lobe of the cerebellum; the fibres of the tract of Gowers originate in the same cells, and those of its fibres which enter the cerebellum do so by its superior peduncle, and these also end in the vermis.

This leaves us still one more set of fibres to consider; these are the fibres that leave the cerebellum and travel up to the brain and down the cord. They, like most of the other tracts, have been investigated by the degeneration method. Their exact course is, however, uncertain, though probably they ultimately terminate by arborising round the multipolar cells of the cerebrum and of the anterior horn of the cord (see fig. 482, p. 660; see also under Cerebellum, Chapter XLIX.).

Reflex Action of the Spinal Cord.

There are two theories of a speculative nature regarding the relationship of reflex and voluntary actions: one is, that all actions are in essence reflex, and that the so-called voluntary actions are modified reflexes, in which the afferent impulse to act, though often obscure, is nevertheless, by seeking, always to be found. Put in popular language, this theory implies that we have really no such thing as a will of our own, but our actions are simply the result of external circumstances.

The other theory is the exact opposite—namely, that all actions are in the beginning voluntary, and become reflex by practice in the lifetime of the individual, or the lifetime of his ancestors, who transmit this character to their descendants.

This is not the place to discuss a philosophical question of this kind, and still less the debated question whether acquired characters are transmissible by inheritance. The distinction between voluntary and reflex actions is a useful practical one, and certainly it cannot be doubted that many practised actions become reflex in the lifetime of every one of us. Take walking, skating, or bicycling as examples: at first these acts of locomotion are those in which the brain is concerned; they are actions demanding the concentration of the attention; but later on the action is largely carried out by the spinal cord, the afferent impulses to the cord from the lower limbs directing the efferent impulses to the muscles concerned.

The reflex actions of the spinal cord may first be studied in a brainless frog, as in this animal the spinal cord possesses a great power of controlling very complex reflex actions.

Reflexes in a Brainless Frog.

After destruction of the cerebrum the shock of the operation renders the animal for a short time motionless and irresponsive to stimuli, but in a few minutes it gradually assumes a position which differs but little from that of a living conscious frog. If thrown into water it will swim; if placed on a slanting board it will crawl up it (Goltz); if stroked on the flanks it will croak (Goltz); if it is laid on its back, and a small piece of blotting-paper moistened with acid be placed on the skin, it will generally succeed in kicking it off; if a foot is pinched it will draw the foot away; if left perfectly quiet it remains motionless. Even when the optic thalami are destroyed also, it still executes complex reflex actions, but all power of balancing and all spontaneity are lost.

The muscular response that follows an excitation of the surface is purposive and constant, the path along which the impulse is propagated being definite.

Under certain abnormal conditions, however, the propagation of the impulse in the cord is widespread, the normal paths being, as it were, broken down. This is seen in the convulsions that occur on slight excitation in animals or men who have suffered from profuse hæmorrhage, or in the disease called lockjaw or tetanus. Such a condition is easily demonstrable in a brainless frog under the influence of strychnine: after the injection of a few drops of a 1 per cent. solution under the skin, cutaneous excitation no longer produces co-ordinated muscular responses, but paroxysms of convulsions, in which the frog assumes a characteristic attitude, with arms flexed and legs extended.

Spreading of reflexes.—If one lower limb is excited, it is that limb which responds: if the excitation is a strong one it will spread to the limb of the opposite side, and if stronger still to the upper limbs also.

Cumulation of reflexes.—This is well illustrated by Turck's method. If a number of beakers of water are prepared, acidulated with 1, 2, 4, etc., parts of sulphuric acid per 1000, and the tips of the frog's toes are immersed in the weakest, the frog at first takes no notice of the fact, but in time the cumulation or summation of the sensory impulses causes the animal to withdraw its feet. If this is repeated with the stronger liquids in succession, the time that intervenes before the muscles respond becomes less and less. This method also serves to test reflex irritability when the frog is under the influence of various drugs.

Inhibition of reflexes.—If, instead of the whole brain, the cerebrum only is destroyed, and the optic lobes are left intact, response to excitation is much slower, the influence of the remaining part of the brain inhibiting the reflex action of the cord. Or if in doing the experiment with acid just described the toes of the other foot are being simultaneously pinched, the response to the acid is delayed. Inhibition, or delay of reflex time is thus produced by other sensations, which, as it were, take up the attention of the cord.

This influence of the brain on the cord is also illustrated in man, by the fact that a strong effort of the will can control many reflex actions. It is, for instance, possible to subdue the tendency to sneeze; if one accidentally puts one's hand in a flame, the natural reflex is to withdraw it: yet it is well known that Cranmer, when being burnt at the stake, held his hand in the flames till it was consumed.

After the spinal cord has been divided by injury or disease in the thoracic region, the brain can no longer exert this controlling action; hence the part of the cord below the injury having it, as it were, all its own way, has its reflex irritability increased.* The increase of reflex irritability is also seen in the disease called *lateral sclerosis;* here the lateral columns, including the pyramidal tract, become degenerated, and so the path from the brain to the cells of the cord is in great measure destroyed. In these patients the increase of reflex irritability may become a very distressing symptom, slight excitations, like a movement of the bed-clothes, arousing powerful convulsive spasms of the legs.

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* In some injuries to the cord produced by crushing, there is a loss of reflexes below the injury. These, however, are not simple transverse lesions; the loss of reflex action is due to extensive injury to grey matter by hæmorrhage.

Reflex time.—In the frog, deducting the time taken in the transmission of impulses along nerves, the time consumed in the cord (reflex time) varies from 0·008 to 0·015 second; if the reflex crosses to the other side it is one-third longer. It is lessened by heat, and under the influence of a strong stimulus (see also p. 204).

Reflex Action in Man.

The reflexes obtainable in man form a most important factor in diagnosis of diseases of the nervous system; each action is effected through an afferent sensory nerve, a system of nerve-cells in the cord termed the reflex centre, and an efferent motor nerve; the whole constitutes what is called the *reflex arc.* The absence of certain reflexes may determine the position in the spinal cord, which is the seat of disease.

Two forms of reflex action must be distinguished:—

1. Superficial reflexes. These are true reflex actions, and are excited by stimulation of the skin.

2. Deep reflexes or tendon reflexes. This is a most undesirable name, as they are not true reflex actions.

Superficial Reflexes.—These are obtained by a gentle stimulation, such as a touch on the skin; the muscles beneath are usually affected, but muscles at a distance may be affected also. Thus a prick near the knee will cause a reflex flexion of the hip.

The most important of these reflexes are:

a. *Plantar reflex:* withdrawal of the feet when the soles are tickled.

b. *Gluteal reflex:* a contraction in the gluteus when the skin over it is stimulated.

c. *Cremasteric reflex:* a retraction of the testicle when the skin on the inner side of the thigh is stimulated.

d. *Abdominal reflex:* in the muscles of the abdominal wall when the skin over the side of the abdomen is stroked; the upper part of this reflex is a very definite contraction at the epigastrium, and has been termed the *epigastric reflex.*

e. A series of similar reflex actions may be obtained in the muscles of the back, the highest being in the muscles of the scapula.

f. In the region of the cranial nerves the most important reflexes are those of the eye—(i) the *conjunctival reflex*, the movement of the eyelids when the front of the eyeball is touched; and (ii) the contraction of the pupil on exposure of the eye to light, and its dilatation on stimulation of the skin of the neck.

Tendon Reflexes.—When the muscles are in a state of slight tension, a tap on their tendons will cause them to contract. The two so-called tendon reflexes which are generally examined are the patella tendon reflex or *knee-jerk*, and the foot phenomenon or *ankle-clonus.*

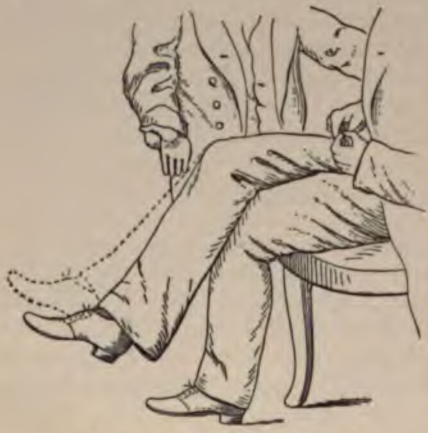

FIG. 488.—The Knee-jerk. (Gowers.)

The knee-jerk.—The quadriceps muscle is slightly stretched by putting one knee over the other; a slight blow on the patella tendon causes a movement of the foot forwards, as indicated in the dotted line of fig. 488. The phenomenon is present in health.

Ankle-clonus.—This is elicited as depicted in the next figure: the hand is pressed against the sole of the foot, the calf muscles are thus put on the stretch and they contract, and if the pressure is kept up a quick succession or clonic series of contractions is obtained. This, however, is not readily obtained in health.

These phenomena are not true reflexes; the time that intervenes between the tap and the response is so short that they must be due to direct stimulation of the muscles by the sudden stretching of their tendons.

Nevertheless, the idea that they are reflex is supported by the following facts:—

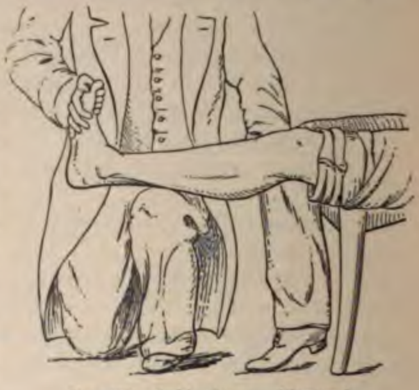

FIG. 489.—Ankle-clonus. (Gowers.)

1. There are nerves in tendon.

2. The phenomena depend for their occurrence on the integrity of the reflex arc. Disease or injury to the afferent nerve, efferent nerve, or spinal grey matter, abolishes them. Thus they cannot

be obtained in locomotor ataxy (damage to the posterior nerve-roots), or in infantile paralysis (damage to the anterior horns of grey matter).

3. They are excessive in those conditions that increase the true reflex irritability, such as severance of brain from cord, and in lateral sclerosis.

How, then, is it possible to reconcile these two sets of facts? The explanation advanced by Sir William Gowers does so best; it is briefly as follows:—

(1) The tendon reflexes are not reflexes, but are due to direct stimulation of the muscle itself.

(2) In order that the muscle may respond, it is necessary that it be in an irritable condition; this is accomplished by putting it slightly on the stretch, and so calling forth the condition called *tonus* (see p. 130), a readiness to contract on slight provocation.

(3) Muscular tonus depends on the integrity of the reflex arc. The sensory stimulus for this reflex muscular tone arises either in the muscle itself, or more probably in the condition of the antagonistic muscles. (See more fully, next paragraph but two).

(4) Hence injury to any part of the reflex arc, by abolishing the healthy tone of a muscle, deprives it of that irritable condition necessary for the production of these so-called reflex actions.

The exact course of the reflex arc concerned in the knee-jerk has been worked out by Sherrington in the monkey. The nerve-fibres are mainly those which pass (1) to and from the crureus by the anterior crural nerve, and (2) to and from the hamstrings by the sciatic nerve. The fibres which supply the crureus arise from the spinal nerve-roots which in man correspond to the 3rd and 4th lumbar; the hamstring supply is from the 5th lumbar and 1st and 2nd sacral roots.

Reciprocal Action of Antagonistic Muscles.—This is an interesting branch of muscle physiology related to the question of tendon reflexes, which we owe to the researches of Sherrington. In brief, he shows that the inhibition of the tonus of a voluntary muscle may be brought about by excitation of its antagonist.

Movement at a joint in any direction involves the shortening of one set of muscles and the elongation of another (antagonistic) set. The stretching of a muscle produced by the contraction of its antagonist may excite (mechanically) the sensorial organs (probably the muscle-spindles, see p. 86) in the muscle that is under extension; in this way a reflex of pure muscular initiation may be started. Experiments show that electrical excitation of the central end of an exclusively muscular nerve produces inhibition of the tonus of its antagonist. For instance, the central end of the severed hamstring nerve is faradised. This nerve contains in the cat 4510 nerve-fibres, and of these about 1810 are sensory in function*; these come from the flexor muscles of the knee, not from the skin. The effect of the stimulation of the nerve on the tonus of the extensor muscles of the knee is seen (*a*) in elongation of those muscles, (*b*) in temporary diminution of the knee-jerk. The experiment may be varied as follows: the exposed flexor muscles detached from the knee, and therefore incapable of mechanically affecting the position of the joint, are stretched or kneaded. This produces a reflex elongation of the extensor muscles of the knee and a temporary diminution of the knee-jerk. The effects are in fact the same as those produced by faradisation of the central end of the nerve supplying them. It may therefore be that reciprocal innervation, which is a common form of co-ordination of antagonistic muscles, is secured by a simple reflex mechanism, an important factor in its execution being the tendency for the action of a muscle to produce its own inhibition reflexly by mechanical stimulation of the sensory apparatus in its antagonist.

On p. 661 we have drawn attention to the three "*nervous circles*" by which an afferent impulse may affect the motor discharge from the anterior horn-cells of the cord; there is the short path by the collaterals of the entering fibre which pass directly to these cells, and there are the two longer paths, *viâ* the cerebellum and cerebrum respectively. In the execution of a voluntary action all three circles are in activity to produce the co-ordination and due contraction and elongation of antagonistic muscles which characterise an effective muscular act. Section of the posterior roots produces not only an inability to carry out reflex actions, but also leads to an inability to carry out effectively those more complicated reflex actions which are called voluntary, and in which the brain participates. Locomotor ataxy, or tabes dorsalis, is a slowly progressive disease, the anatomical basis of which is a degeneration of the nerve-units of the spinal ganglia. It is, therefore, analogous to a physiological experiment in which the posterior roots are divided, and although fibres may remain which still allow of the passage of nervous impulses, the action of the three circles is greatly interfered with; the spinal reflex arc is at fault; this is shown by the loss of reflex action, the disappearance of the tendon reflexes, and the want of tonus in antagonistic muscles; the main symptom of the disease is want of muscular co-ordination, and this is produced not only by the lesion in the spinal cord, but is accentuated by the want of continuity in the other two circles, so that the brain is unable to effectively control the motor discharge from the anterior cornual cells.

The tendon phenomena are important to the pathologist; they furnish him with a valuable means of diagnosis in nervous disorders.

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* The number of sensory nerve-fibres is determined by counting the healthy fibres in the nerves after section of the anterior nerve-roots.

Their usefulness in the normal state is very well put by Starling in the following words:—"Every joint is protected by inextensible ligaments and by muscles. A sudden strain on a ligament will rupture some of its fibres, and perhaps injure the joint surfaces. An ordinary reflex contraction could not prevent this, for the mischief would be done before the reaction could take place. But the central nervous system keeps the muscles awake, so that they themselves may react to any sudden increase in the tension by an equally sudden contraction which saves the joint before the central nervous system has had time to become aware of the strain."

Reaction Time in Man.—The term reaction time is applied to the time occupied in the centre in that complex response to a pre-arranged stimulus in which the brain as well as the cord comes into play. It is sometimes called the *personal equation*. It may be most readily measured by the electrical method, and the accompanying diagram (fig. 490) will illustrate one of the numerous arrangements which have been proposed for the purpose.

In the primary circuit two keys *A* and *B* are included, and a chronograph (1), arranged to write on a revolving cylinder (fast rate). Another chronograph (2), marking 1-100ths of a second, is placed below this. The experiment is performed by two persons *C* and *D*. The key *A*, under the control of *C*, is opened. The key *B*, under the control of *D*, is closed. The electrodes *E* are applied to some part of *D*'s body. *C* closes *A*. The primary circuit is made, and the chronograph moves. As soon as *D* feels the shock he opens *B*, the current is thus broken, and the chronograph lever returns to rest. Measure the time between the two movements of the chronograph (1), by means of the time tracing written by chronograph (2). From this, the time occupied by transmission along the nerves has to be deducted, and the remainder is the *reaction time*. It usually varies from 0·15 to 0·2 second, but is increased in :—

The Dilemma.—The primary circuit is arranged as before. Lead the wires from the secondary coil to the middle screws of a reverser without cross wires. To each pair of end screws, attach a pair of electrodes *E* and *E'*, applied to different parts of *D*'s body (fig. 491).

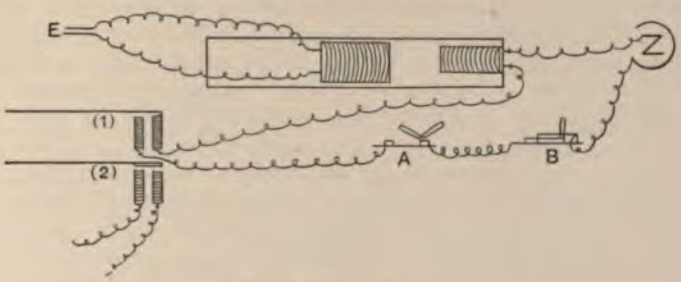

FIG. 490.—Reaction time.

Arrange previously that *D* is to open *B*, when one part is stimulated, but not the other, *C* adjusting the reverser unknown to *D*. Under these circumstances the reaction time is longer.

The reaction time in response to various kinds of stimuli, sound, light, pain, etc., varies a good deal; the condition of the subject of the experiment is also an important factor. This, however, is really a practical branch of psychology, and has recently been much worked at by students of that science (see also p. 204).

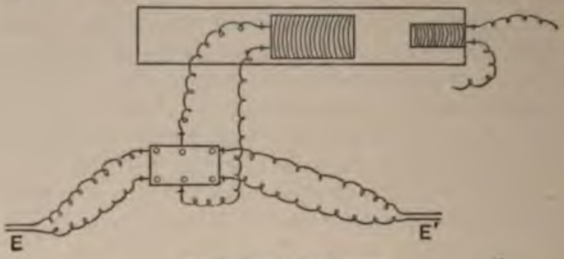

Fig. 491.—The Dilemma.

Spinal Visceral Reflexes.

The spinal grey matter contains centres which regulate the operation of certain involuntary muscles. Some of these centres are:—

The *cilio-spinal* centre controls the dilatation of the pupil; it is situated in the lower cervical region, reaching as far down as the origin of the first to the third thoracic nerve.

Subsidiary *vaso-motor* centres. The principal vaso-motor centre is situated in the bulb, and subsidiary centres are scattered through the spinal grey matter (see p. 299).

The same is probably true for all the muscular viscera, but particular study has been directed to those in the pelvis, and centres for *micturition, defæcation, erection,* and *parturition* are contained in the lumbo-sacral region of the cord. If the spinal cord is cut through above the situation of these centres, the result is in general terms that any influence of the higher (voluntary) centres over these actions is no longer possible. The actions in question are then simply reflex ones occurring unconsciously at certain intervals, and set in movement by the peripheral stimulus (fulness of bladder, or of rectum, etc.). If the portion of the cord where these centres are placed is entirely destroyed, the result is paralysis of the muscles concerned, though in certain cases, even after such a severe injury, some amount of recovery has been noticed, which must be attributed to the peripheral ganglia being able to play the part of reflex centres.

The viscera are supplied not only by efferent (motor and inhibitory) nerves, but are connected to the central nervous system by certain afferent channels, namely (1) the vagus; (2) the spinal roots from the thoracic and first two lumbar nerves; and (3) the second, third, and fourth sacral roots. Under normal circumstances, the afferent impulses do not rise into consciousness, and even on injury pain is often absent. In disease where they are stirred up to excessive action, as in various forms of colic, the pain, however, may be intense. A good deal of pain is usually "referred" to skin areas which are "tender," and Ross's suggestion that the pain in such cases is referred to parts supplied by sensory cutaneous fibres ending in the same segments of the cord as do the afferent fibres from the viscera in question, has been amplified and placed beyond doubt by Head's researches.

Bladder Reflexes.—The spinal region which acts as the micturition centre is that with which the first, second, and third lumbar, and the second, third, and fourth sacral roots are connected. Transverse section of the cord about the level of the sixth lumbar segment (in cat and rabbit) causes immediate escape of urine from the bladder. In the first days after the operation the bladder can only be emptied by artificial stimulation, and especially easily by a light quick pressure on the distended bladder through the abdominal walls. It is not the pressure that squeezes out the urine, it merely sets going a reflex in which contraction of the detrusor and relaxation of the sphincter constitute the final stage. Later on the urine is voided "spontaneously" at intervals, and this is usually accompanied by defæcation.

Goltz and Ewald found in dogs in which the lower part of the cord had been totally removed, that the bladder emptied itself spontaneously from time to time months later, but usually the bladder had to be emptied by artificial means. In man retention of urine is a common and usually a permanent symptom after a total transverse lesion of the cord.

Defæcation.—A regular expulsion of fæcal matter occurs without difficulty in animals after transverse section of the cord in the upper lumbar region. The tone of the external sphincter is generally recovered a few minutes after the operation; and in Goltz and Ewald's dogs the tonus returned even when the lower part of the cord was entirely removed. After a total transverse lesion of the cord in man, incontinence of fæces is usually described, but this is not the case in monkeys. Gowers describes two states in disease which can be distinguished by introducing the finger into the rectum: (1) if the centre is inactive a momentary contraction caused by local irritation of the sphincter is followed by permanent relaxation; (2) relaxation is followed by gentle tonic contraction: in such cases the reflex centre and its nerves are intact.

Uterine Reflexes.—Uterine contractions can be induced by rectal injections, the passage of a foreign body into the uterus, the application of the child to the breast, and by other means. In animals faradisation of the central end of the first sacral nerve produces the same result. The contractions of the uterus are therefore reflex. Several cases have been recorded in which parturition has occurred normally in women who have had the cord divided across completely in the thoracic region; it is thus evident the centre must be a lumbar one. In such cases the uterine contractions technically called "pains" are strong, but pain is, of course, absent. The communication with the lumbar region appears to be principally by the first three lumbar nerves. Similar observations have been made experimentally in animals, and in one of Goltz and Ewald's dogs in which the cord had been removed from the lower thoracic region downwards, pregnancy followed coitus, and terminated with successful parturition. The mammary glands enlarge as usual in such cases, even when, as in Routh's well-known case (where the cord was completely destroyed at the seventh thoracic segment), there can be no spinal communication between the pelvis and the breast.

Erection.—This reflex can be excited in man even immediately after a total transverse lesion of the cord; so also can ejaculation, but not so commonly. The evidence in favour of such acts being spinal reflexes is very complete in the case of animals.

CHAPTER XLVIII

FUNCTIONS OF THE CEREBRUM

The brain is the seat of those psychical or mental processes which are called volition and feeling; volition is the starting-point in motor activity; feeling is the final phase of sensory impressions.

In the days of the ancients very curious ideas prevailed as to the use of the brain. It is true that Alkmäon, as early as 580 B.C., placed the seat of consciousness in the brain, but this view was of the nature of a guess, and did not meet with general acceptance; and two hundred years later Aristotle considered that the principal use of the brain was to cool the hot vapours rising from the heart. At this time the seat of mental processes, especially those of an emotional kind, was supposed to be in the heart, an idea now confined to poets; or in the bowels, as those acquainted with such ancient writings as the Bible will know.

As time went on, truer notions regarding the brain came to the fore: thus Herophilus (300 B.C.) was aware of the danger attending injury to the medulla; Aretæus and Cassius (97 A.D.) knew that injury to one side of the brain produced paralysis of the opposite side of the body; and Galen (131—203 A.D.) was acquainted with the main motor and sensory tracts in brain and cord. Between that time and this, most of the celebrated anatomists have contributed something to our knowledge, and one may particularly mention Vesalius, Sylvius, Rolando, Gall, Carus, Willis, and Burdach; many of these names are familiar because certain structures in the brain have been christened after them. The erroneous notion that the brain was not excitable by stimuli lasted even to the days of Flourens and Magendie.

Effects of Removal of the Cerebrum.

When the brain is removed in a frog, it is deprived of volition and of feeling; it remains perfectly quiescent unless stimulated; it is entirely devoid of initiatory power, but, as we have already seen, it will execute reflex actions, many of which are of a complex nature (see p. 669 and also Chapter L).

A pigeon treated in the same way remains perfectly motionless and unconscious unless it is disturbed (see fig. 492). When disturbed in any way it will move; for instance, when thrown into the air it will fly; but these movements are, as in the frog, purely reflex in character.

In mammals the operation of extirpation of the brain is attended with such severe hæmorrhage that the animal dies very rapidly, but in some few cases where the animals have been kept alive, the phenomena they exhibit are precisely similar to those shown by a frog or pigeon. In the case of the dog, portions of the cortex have been removed piecemeal by Goltz of Strasburg, until at last the whole of the cortex has been extirpated. Such animals carry out co-ordinated movements of a complicated character very well, but they manifest no intelligence, and have complete lack of memory. They are in a condition analogous to that of the frogs and pigeons just mentioned.

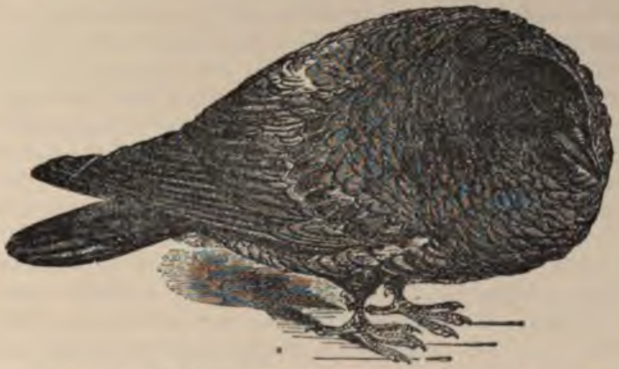
FIG. 492.—Pigeon after removal of the hemispheres. (Dalton.)

Localisation of Cerebral Functions.

When the main function of the cerebrum was understood, physiologists were divided into two schools; those who thought that the brain acted as a whole, and those who thought that different parts of the brain had different functions to perform. One of the most prominent of the first school was Flourens; and Goltz, whose work has been done chiefly on dogs, is the only eminent living survivor of this set of physiologists. Gradually, as better methods have come in, and especially since monkeys have been used for experiment, those who believe in the localisation of function have multiplied; and now, localisation of cerebral function is more than a theory, it is an accepted fact. Perhaps the best practical evidence of this is the fact that experiments on monkeys have been taken as the basis for surgical operations on the human brain, and with perfect success.

The earliest to work in the direction of localisation were Hitzig and Fritsch. The subject was then taken up by Ferrier and Yeo, and later by Schäfer, Horsley, etc., in this country, and by Munk and many others in Germany. In addition to those who have studied the matter from the experimental standpoint, must also be reckoned the pathologists, who in the *post-mortem* room have examined the brains of patients dying from cerebral disease, and carefully compared the position of the disease with the symptoms exhibited by the patients during life. In this way two series of independent investigations have led to the same results; both methods are essential, as many minor details discovered by the one method correct the erroneous conclusions which are apt to be drawn by those who devote their entire attention to the other.

The main point which these researches have brought out is the overwhelming importance of the cortex; it contains the highest cerebral centres. Before Hitzig began his work, the corpus striatum was regarded as the great motor centre, and the optic thalamus as the chief centre of sensation; very little note was taken of the cortex; it appears to have been almost regarded as a kind of ornamental finish to the brain. The idea that the basal ganglia were so important arose from the examination of the brains of people who had died from, or at least suffered from, cerebral hæmorrhage.

The most common situation for cerebral hæmorrhage is either in the region of the corpus striatum or optic thalamus; it was noticed that motor paralysis was the most marked symptom if the corpus striatum was injured, and sensory paralysis if the optic thalamus was injured. The paralysis, however, is due, not to injury of the basal ganglia, but of the neighbouring internal capsule. The internal capsule consists in front of the motor fibres passing down from the cortex to the cord, and behind of the sensory fibres passing up from cord to the cortex (see p. 655). Hence, if these fibres are ploughed up by the escaping blood, paralysis naturally is the result. If a hæmorrhage or injury is so limited as to affect the basal ganglia only, and not the fibres that pass between them, the resulting paralysis is slight or absent.

The question will next be asked: What, then, is the function of the basal ganglia? They are what we may term subsidiary centres: the corpus striatum, principally in connection with movement, and the optic thalamus, in connection with sensation, and especially with the sense of vision as its name indicates.

A subsidiary centre may be compared to a subordinate official in an army. The principal centre may be compared to the commander-in-chief. This highest officer gives a general order for the movement of a body of troops in a certain direction; we may compare this to the principal motor-centre of the cortex sending out an impulse for a certain movement in a limb. But the general does not give the order himself to each individual soldier, any more than the cerebral cortex does to each individual muscle; but the order is first given to subordinate officers, who arrange exactly how the movement shall be executed, and their orders are in the end distributed to the individual men, who must move in harmony with their fellows with regard to both time and space. So the subsidiary nerve-centres or positions of relay enable the impulse to be widely distributed by collaterals to numerous muscles which contract in a similar orderly, harmonious, and co-ordinate manner.

There is just the same sort of thing in the reverse direction in the matter of sensory impulses. Just as a private in the army, when he wishes to communicate with the general, does so through one or several subordinate officers, so the sensory impulse passes through many cell-stations or subsidiary centres on the way to the highest centre, where the mental process called sensation, that is, the appreciation of the impulse, takes place.

There are two great experimental methods used for determining the function of any part of the cerebrum. The first is **stimulation**; the second is **extirpation**. These words almost explain themselves; in *stimulation* a weak interrupted induction current is applied by means of electrodes to the convolution under investigation, and the resulting movement of the muscles of the body, if any occurs, is noticed. In *extirpation* the piece of brain is removed, and the resulting paralysis, if any, is observed.

It is essential, when the experiment of stimulating the cortex of the brain is being performed, that the animal should be anæsthetised, otherwise voluntary or reflex actions will occur which mask those produced by stimulation. If, however, the animal is too deeply under the influence of a narcotic the brain is inexcitable.

On p. 379 Ehrlich's experiments with methylene blue are described. In an anæsthetised animal the brain is inactive, and if the pigment is injected into the blood, the brain is seen to be of a blue colour. If, however, a spot of the cerebral surface is stimulated, that part of the brain is thrown into action, oxygen is used up, and the methylene blue is reduced, and in consequence that area of the brain loses its blue tint. If the animal is so deeply narcotised that the brain does not discharge an impulse, the part stimulated remains blue.

By such means the cortex has been mapped out into what we may provisionally term motor areas, and sensory areas.

Motor areas.—These areas are also termed *sensori-motor* or *kinæsthetic*, for reasons which will be explained more fully later. The name *Rolandic area* which they have also received is derived from their anatomical position.

Stimulation of them produces movement of some part of the opposite side of the body; excitation of the same spot is always followed by the same movement in the same animal. In different animals excitation of anatomically corresponding spots produces similar or corresponding results. It is this which has enabled one to apply the results of stimulating areas of the monkey's brain to the elucidation of the function of the similar brain of man.

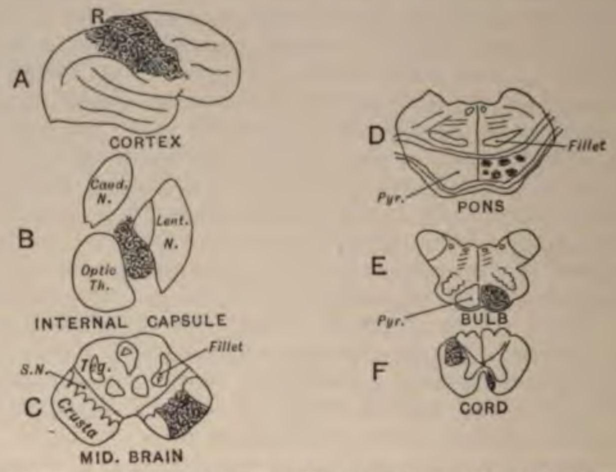

Fig. 493.—Degeneration after destruction of the Rolandic area of the right hemisphere. (After Gowers.)

If the stimulation used is too powerful the result is a movement of other parts, and a considerable portion of the body may be thrown into convulsive movements similar to those seen in epilepsy.

Extirpation, or removal, of these areas produces paralysis of the same muscles which are thrown into action by stimulation.

The degeneration tracts after destruction of the Rolandic area are shown in fig. 493.

The shaded area in each case represents the injured or degenerated material; A in the cortex, B in the anterior part of the posterior limb of the internal capsule, C in the middle of the crusta of crus and mid-brain, D in the pyramidal bundles of the pons, E in the pyramid of the bulb, and F in the crossed and direct pyramidal tracts of the cord.

Sensory areas.—*Stimulation* of these produces no direct movements, but doubtless sets up a sensation called a *subjective* sensation; that is, one produced in the animal's own brain, and this indirectly leads to movements which are reflex; thus on stimulating the auditory area there is a pricking up of the ears; on stimulating the *visual area* there is a turning of the head and eyes in the direction of the supposed visual impulse. That such movements are reflex and not direct is shown by the long period of delay intervening between the stimulation and the movement.

Extirpation of a sensory area leads to loss of the sense in question.

The rougher experiments performed by nature in the shape of diseases of the brain produce corresponding results.

Some diseases are of the nature of extirpation.

An instance of this is cerebral hæmorrhage. If the hæmorrhage is in the region of the internal capsule, it cuts through fibres to the muscles of the whole of the opposite side of the body, as they are all collected together in a narrow compass, and the condition obtained is called *hemiplegia*. The varieties of hemiplegia are numerous, according as motor or sensory fibres are most affected, and in one variety of hemiplegia, called *crossed hemiplegia*, the face is paralysed on one side of the body, the limbs on the other; this is due to injury of the nerve-tracts in the bulb, subsequent to the crossing of the fibres to the nucleus of the seventh nerve, but above the crossing of the pyramids.

If now the hæmorrhage occurs on the surface of the brain, a much more limited paralysis, called *monoplegia*, is the result; if the arm area is affected, there will be paralysis of the opposite arm; if the leg area, of the opposite leg; if a sensory area, there will be loss of the corresponding sense.

Some diseases, on the other hand, act as the induction currents do in artificial stimulation; they irritate the surface of the brain; such a disease is a tumour growing in the membranes of the brain; if the tumour irritates a piece of the motor area, there will be involuntary movements in the corresponding region of the body; these movements may culminate in the production of epileptiform convulsions commencing in the arm, leg, or other part of the body which corresponds to the brain area irritated. It is these cases of "*Jacksonian Epilepsy*" which have given the best results in surgery; the movement produced is an indication of the area of the brain which is being irritated, and the surgeon after trephining is able to remove the source of the mischief. If the area of the brain which is irritated is a sensory area, the result produced is a subjective sensation, similar to what we imagine is produced in animals with an electric current.

We may now proceed from these general considerations to particular points, and give maps of the brain to show the areas we have been speaking of.

Figs. 494 and 495 are views of the dog's brain. It is convenient to take this first because it was the starting-point of the experimental work on the subject in the hands of Hitzig and Fritsch. If the text beneath the figure is consulted, it will be seen that the motor areas, mapped out by the method of stimulation, are situated in the neighbourhood of the *crucial sulcus*, which corresponds to the fissure of Rolando in man.

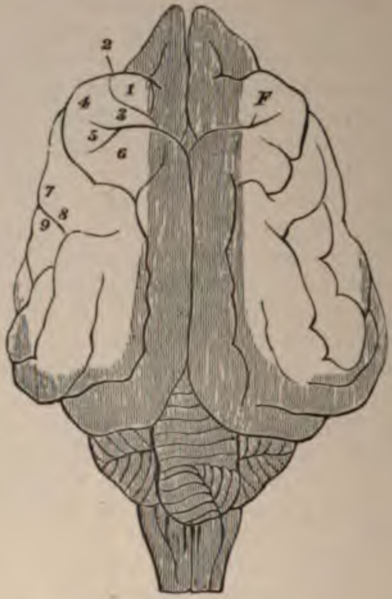

FIG. 494.

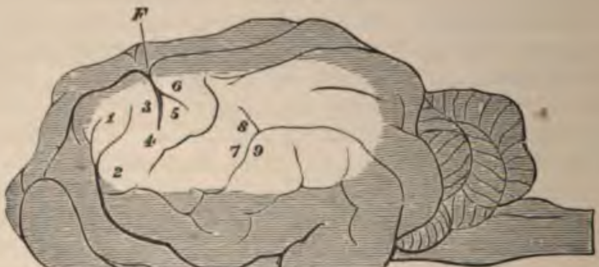

FIG. 495.

FIGS. 494 and 495.—Brain of dog, viewed from above and in profile. *F*, frontal fissure, sometimes termed crucial sulcus, corresponding to the fissure of Rolando in man. *S*, fissure of Sylvius, around which the four longitudinal convolutions are concentrically arranged; 1, flexion of head on the neck, in the median line; 2, flexion of head on the neck, with rotation towards the side of the stimulus; 3, 4, flexion and extension of anterior limb; 5, 6, flexion and extension of posterior limb; 7, 8, 9, contraction of orbicularis oculi, and the facial muscles in general. The unshaded part is that exposed by opening the skull. (Dalton.)

Coming next to the brain of the monkey, figures 496 and 497 are reproductions from Ferrier. He marked out the surface into a number of circles, stimulation of each of which produced movements of various sets of muscles, face, arm, and leg from below upwards; extirpation of these same areas produced the corresponding paralysis. It will be further noticed that these areas are all grouped around the fissure of Rolando, particularly in the ascending frontal and ascending parietal convolutions; hence the term *Rolandic area* which is often applied to this region of the brain.

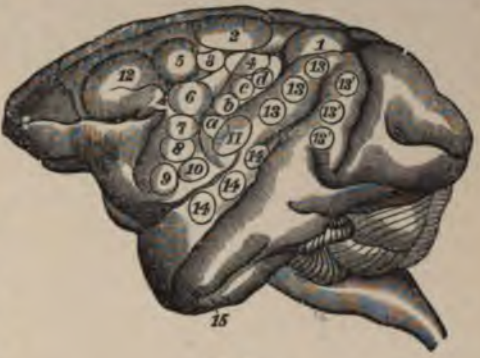

FIG. 496.

Most of our knowledge concerning the localisation of the sensori-motor area in the human brain has been deduced from experiments on the lower monkeys. Valuable as such knowledge is, infinitely more useful knowledge, from the standpoint of the human brain, would be obtained by examining the brains of those monkeys nearest to man, which are known as the anthropoid apes. The difficulty and expense of obtaining such animals has hitherto deterred investigators from performing such experiments. Horsley and Beevor examined the brain of an orang-outang some years ago, and now Sherrington and Grünbaum have made a number of experiments; several specimens of two species of chimpanzee, the orang and the gorilla, have been examined. Their conclusions are of great importance. The figure on p. 687 (fig. 498) of the chimpanzee's brain shows what has been found; the orang and the gorilla gave practically the same results, and no doubt the human brain would give identical results also if it could be examined.

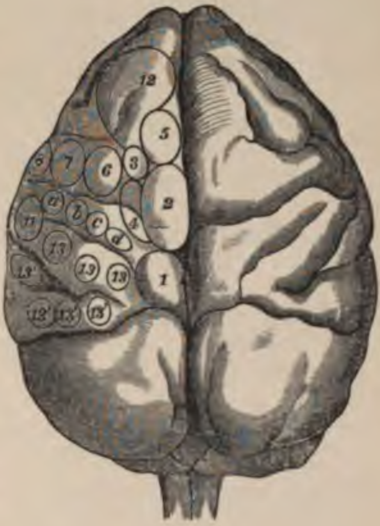

FIG. 497.

FIGS. 496 and 497.—Diagrams of monkey's brain to show the effects of electric stimulation of certain spots. (According to Ferrier.)

The method used is to expose the brain in an anæsthetised animal, and thoroughly explore it with a weak faradic current, one electrode being placed on the brain, and the other attached to an indifferent part of the animal's body. This allows of finer localisation than is possible with the ordinary double-point electrodes.

The so-called "motor" area includes continuously the whole length of the ascending frontal, or as it is sometimes called, the precentral convolution. It never extends behind the central sulcus, or, as it is sometimes called, the fissure of Rolando. On the mesial surface it extends but a short distance, and never as far as the calloso-marginal fissure. The motor area extends also into the depth of the Rolandic and other fissures; the part of the excitable area thus hidden equals or may even exceed that on the free surface of the hemisphere. The arrangement of the various regions of the musculature follow the segmental sequence of the cranio-spinal series to a remarkable extent; in fact, the excitable area may be compared to the spinal cord upside down. The accompanying figure indicates this better than any verbal description.

The sulci in the region of the cortex dealt with cannot be considered to act as physiological boundaries, and the variations in the sulci in these higher brains are so great that they prove to be precarious or even fallacious landmarks to the details of the true topography of the cortex.

It cannot fail to strike even a superficial observer how large the cortical area is that deals with movements of the head and arm regions when compared with that of the lower limb, and still more with that of the trunk. The trunk itself has a larger mass of muscular tissue, but it is in the head region (which includes the complex movements of the tongue and such structures as the vocal cords) and in the arm and hand that the movements are most varied and most delicate. No doubt this is the explanation of the greater size of their cortical representation.

The experiments of extirpation confirm those of stimulation; for example, extirpation of the hand area is followed by severe paralysis of the hand, but in a few weeks use and power return in a remarkable degree. On the other hand, ablations of even larger portions of the parts behind the Rolandic fissure do not give rise to even transient paralysis, and do not lead to degeneration in the pyramidal system of fibres.

Sherrington and Grünbaum also found that the part of the frontal region which yields conjugate movements of the eyeballs is separated from the Rolandic area by a field of "inexcitable" cortex. As to the occipital lobe, only from its extreme posterior apex did faradisation yield any movement of the eyes, and then not easily. This becomes intelligible on histological examination; the large motor cells in the deeper layer of the grey matter are so scattered that they are called "solitary cells"; their axons pass to the oculo-motor nuclei, and so the pathway is provided for the movements of the eyes in accordance with the necessities of vision.

The marginal convolution on the mesial surface of the hemisphere was first investigated by Schäfer and Horsley, in the lower monkeys. They found in these animals that it contained a considerable extension of the "motor" area, including the cortical centres for the trunk muscles. This, at any rate, is not the case for the higher apes, and therefore probably is not true for man.

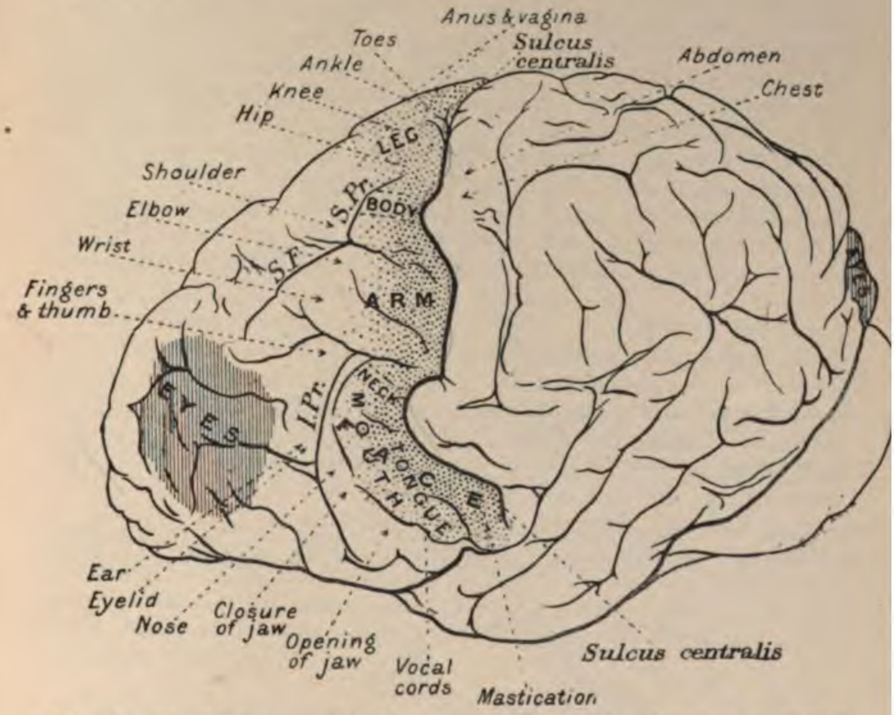

FIG. 498.—Brain of Chimpanzee. Left hemisphere viewed from side and above so as obtain the configuration of the Rolandic area. The figure involves some foreshortening about both ends of the sulcus centralis or fissure of Rolando. The extent of the so-called motor area on the free surface of the hemisphere is indicated by black stippling which extends back to the central sulcus. Much of the "motor" area is hidden in sulci; for instance, it extends into both the central and precentral sulci. The names printed in capitals on the stippled area indicate the main subdivisions of the "motor" area; the names printed small outside the brain indicate by their pointing lines some of the chief subdivisions of the main areas. But there is much overlapping of the areas which it is not possible to indicate in a diagram of this kind. The shaded regions marked "eyes" in the frontal and occipital regions indicate the areas which under faradisation yield conjugate movements of the eyeballs. They are marked in vertical shading instead of stippling, as is the "motor" area. S.F.=superior frontal sulcus. S.Pr.=superior precentral sulcus. I.Pr.=inferior precentral sulcus. (After Sherrington and Grünbaum.)

In experiments on unilateral extirpation in animals, and in destructive lesions of one side of the brain in man, it is the muscles which act normally unilaterally which are most paralysed. The muscles which normally move bilaterally, *e.g.* the chest muscles in breathing, the trunk muscles in maintaining an erect position, are comparatively little affected; the spinal centres of such muscles are no doubt connected by commissural fibres, and therefore can be affected from both sides of the brain.

The following diagram is an instructive one indicating the relative positions of the principal motor fibres in their course from cortex to the crus. The letterpress beneath it should be carefully consulted.

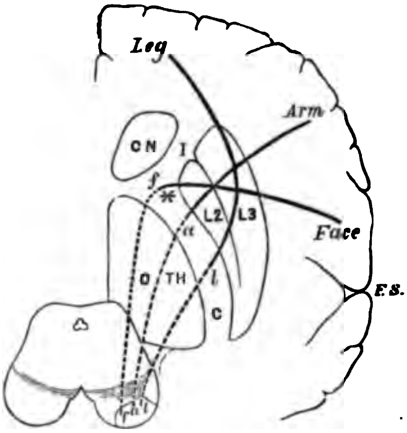

FIG. 499.—Diagram to show the relative positions of the several motor tracts in their course from the cortex to the crus. The section through the convolutions is vertical; that through the internal capsule, I, C, horizontal; that through the crus also horizontal. C.N., caudate nucleus; O.TH., optic thalamus; L2 and L3, middle and outer part of lenticular nucleus; *f*, *a*, *l*, face, arm, and leg fibres. The words in italics indicate corresponding cortical centres; F.S., fissure of Sylvius. (Gowers.)

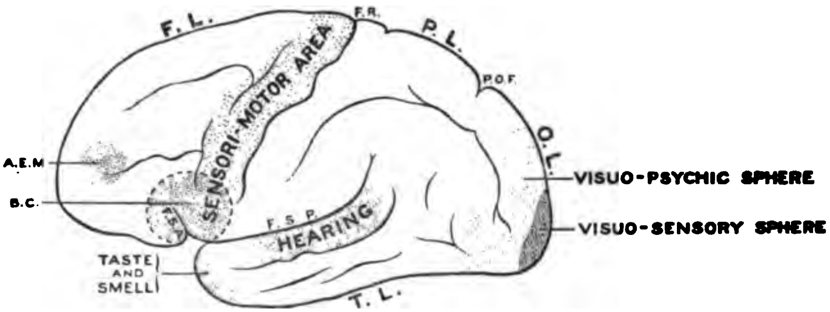

FIG. 500.—Left cerebral hemisphere, outer surface. The lobes and the principal sulci are indicated by their initial letters; A.E.M., anterior centre for eye movements; B.C., Broca's convolution.

The Speech Centre.—Fig. 500 is an outline map of the left cerebral hemisphere in man. The speech centre is surrounded by a dotted circle. There are other centres concerned in speech, as we shall see when considering the question of association fibres (p. 695); but this is the centre for the muscular actions concerned in speech. The discovery of this centre was the earliest feat in the direction of cerebral localisation. It was discovered by a French physician named *Broca;* he noticed that patients who died after hæmorrhage in the brain, but who previous to death exhibited a curious disorder of speech called *aphasia,* were found, after death, to have the seat of the hæmorrhage in this convolution. The convolution is generally called *Broca's convolution.* Experiments on animals are useless in discovering the centre for speech. Sherrington and Grünbaum found in the higher apes that faradisation of the Broca area does not evoke vocalisation.

The most curious fact about the speech-centre is that it is unilateral; it is situated only on the left side of the brain, except in left-handed people, where it is on the right. We are thus left-brained so far as the finer movements of the hand-muscles are concerned, as in writing, and we are also left-brained in regard to speech, an action intimately associated with writing.

The visual area is in the occipital lobe. Removal of one occipital lobe in a monkey, or disease of that lobe in man, produces blindness of the same side of each retina, or inability to see the opposite half of the visual field. This is called *hemianopsia;* the head and eyes are turned to one side (*conjugate deviation* to the side of the injury). Such an operation does not destroy vision in the central portion (*macula lutea*) of either retina, because each macula sends impulses to both sides of the brain. The macula is found only in monkeys and man. Stimulation of one visual area leads to a subjective sensation apparently coming from the same halves of both retinæ, and also excites the motor cells (solitary cells, see p. 686); this produces *conjugate deviation of head and eyes* towards the opposite side to that stimulated.

The optic radiations consist of (1) sensory fibres from the optic tracts *via* the external geniculate bodies; (2) motor fibres to the centres for eye-movements; and (3) association fibres which are last developed. The last named link one convolution to others, and the two hemispheres together, and bring about association of ideas of vision in both hemispheres, and with other sensations. A large collection of such fibres runs horizontally through the grey matter. This white stripe is visible to the naked eye; it is the anatomical mark of the *visuo-sensory cortex,* and is called the *line of Gennari.* The growth of the great parietal association centre pushes the visuo-sensory area in man mainly on to the mesial surface of the hemisphere (see area 4 in figs. 506, 507, p. 696). The *visuo-psychic* region (fig. 500) has no line of Gennari, but possesses many pyramidal cells in its outer layers, which play the part of association units where memory pictures are stored and visual sensations correlated with those from other sense-organs; the higher one ascends the animal scale, the greater becomes the depth of this layer. The eye centre in the frontal lobe is separated, as in the higher apes, by inexcitable grey matter from the rest of the sensori-motor area. In the lower monkeys the anterior eye centre is not insulated in this way. No cortical centre is purely motor or purely sensory, and this one, though usually called motor, has its sensory complement probably from the eyeballs and eyelids (5th nerve). The newly developed grey matter between it and the Rolandic region is an area probably concerned in the association of eye movements with equilibration and the maintenance of the erect position; we know that the fibres from the frontal lobe to the cerebellum are very numerous.

The auditory area is in the posterior part of the upper temporal convolution, and is connected to the visual by annectent gyri. **Taste and smell** are closely connected; their cerebral area is in the uncinate convolution and tip of the temporal lobe. This part is enlarged in animals with a keen sense of smell.

Munk's view, supported in this country by Bastian, Mott, and numerous others, is that the sensory fibres from the skin and muscles terminate in the Rolandic area; and the histological researches of Golgi and Ramon y Cajal (see figs. 479 and 482) point to the same conclusion. This is, in fact, what one would expect; volition and feeling are associated together so closely physiologically, that anatomically we should expect to find the commencement of the volitional fibres contiguous to the terminations of the sensory fibres. That this is really the case has been shown by a careful examination of the sensation in animals in which the Rolandic area has been removed, and in cases of hemiplegia in man. A delicate test is to place a clip on the fingers or toes, taking care the animal does not see the clip put on. If there is loss of tactile sensibility the monkey either takes no notice at all of the clip or removes it after a long delay. Whereas if sensation is perfect the monkey at once seizes the clip and flings it away. It is found that the intensity of both the motor and sensory paralysis are directly proportional to each other. Hence the term motor area, which we have been provisionally employing for the Rolandic area, should be replaced by the more correct term **sensori-motor** or **kinæsthetic area**. These new terms indicate that what really occurs in the Rolandic area is a sense of movement, and this acts as a stimulus *viâ* the pyramidal tracts to the true motor centres which are in the opposite anterior horn of the spinal cord. If the posterior roots of the spinal nerves are divided there is a loss of sensation, and so the sense of movement cannot reach the brain from the muscles, and consequently the muscles are not called into action; when all the posterior roots coming from a limb in a monkey are cut, the muscles, so far as voluntary movements are concerned, are in fact as effectually paralysed as if the anterior roots of the spinal nerves had been cut. The muscles, however, do not degenerate as they would if the anterior roots had been cut. They merely undergo a small amount of wasting due to want of use ("disuse atrophy").

Prof. Schäfer is one prominent worker who has not accepted Munk's views on this subject. He still regards the Rolandic area as essentially motor in function. Naturally, he does not deny that it has connections with sensory fibres, but he considers it incorrect to speak of the area as a sensory one. He has produced injuries of the area without obtaining any loss of sensation, and in testing the sensations of his monkeys employs the method of stroking the skin, which he regards as more trustworthy than Schiff's clip test. The sensory disturbances observed by others he regards as due to general disturbance of the brain produced by the severity of the operation.

On referring once more to the maps of the brain, it will be seen that there are many blanks; one of these is in the anterior part of the frontal region. Extirpation or stimulation of this part of the brain in animals produces but little result. The large size of this portion of the brain is very distinctive of the human brain, and it has therefore been supposed that here is the seat of the higher intellectual faculties. Such a question is obviously very difficult to answer by experiments on animals. Both experimental physiology and pathology have localised the sensory areas (and sensations are the materials for intellect) either within or behind the Rolandic area, but this does not necessarily mean that the frontal convolutions have nothing to do with intellectual functions. The celebrated American crowbar accident is generally quoted as a proof to the contrary; owing to the premature explosion of a charge of dynamite in one of the American mines a crowbar was sent through the frontal region of the foreman's head, removing the anterior part of his brain. He is usually stated to have subsequently returned to his work, without any noteworthy symptoms. Recent examination of the records of the case has shown that this is not correct; when he returned to work he was practically useless, having lost just those higher functions which are so important in the superintendence of other people. Mott's observations on lunatics show that this region is important for intellectual operations, though not so important as the parietal association area behind the Rolandic area; the greater the intellectual development, the larger and more convoluted does this parietal region become.

The association fibres have been the subject of special study by Flechsig, who has shown that in the development of the brain these are the last to become myelinated; white fibres do not become fully functional until they receive their medullary sheath. This coincides with the well-known fact that association of ideas is the last phase in the psychical development of the child. It has been shown that the frontal convolutions are connected by important association tracts with the more posterior regions of the brain, and that there is therefore no difficulty in understanding that the frontal convolutions play the part of a centre for the association of ideas, or in other words for intellectual operations.

Function and Myelination.

Flechsig's embryological method has given us most valuable knowledge of the structure and functions of the human brain. The method depends on the fact that various tracts of fibres become myelinated, *i.e.*, acquire their medullary sheath at successive periods of time in development. The myelin sheath appears three or four months after the axis cylinder is formed. The Weigert method of staining renders the detection of a medullary sheath an easy task. Flechsig's method is in short the reverse of the Wallerian method. In the former method the tracts are isolated by the differences in the origin of the myelin sheath; in the latter method, the same object is obtained by observing the degeneration which is most noticeable in the same sheath.

In the central nervous system, the afferent projection fibres are myelinated first; the efferent projection fibres and the association fibres are myelinated later. Thus in the human fœtus the peripheral nerves and nerve-roots become myelinated in the fifth month of intra-uterine life; of the tracts in the cord, those of Burdach and Goll (*exogenous* fibres springing from the cells of the spinal ganglia) are the first to be myelinated; next come the tracts of Flechsig (dorsal cerebellar) and of Gowers (ventral cerebellar): these are *endogenous* fibres springing from cells within the cord. All these tracts are afferent. The pyramidal tracts, the great efferent or motor channels, are not myelinated until after birth. The whole afferent tract is myelinated at birth; these fibres have *in utero* been exercised in conveying impressions to the afferent reception centres, the stimuli arising from contact of the fœtal integuments with the maternal tissues. There is also early myelination around the calcarine fissure in the visual sphere, and in connection with the areas related to other special senses. This is shown in figs. 501 and 502, where the condition at birth and that some months later are compared.

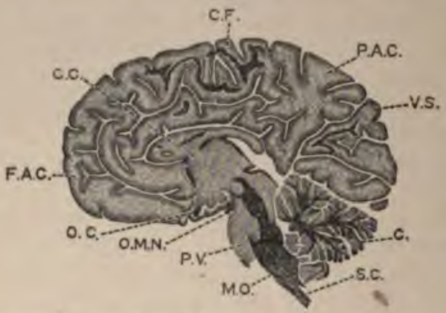

FIG. 501.—Diagram of vertical section through brain of new-born child, drawn from one of Flechsig's photographs. The section was treated by Weigert's method, by which myelinated fibres are deeply stained. Attention is drawn to the deep shading indicating myelination around the central fissure, which corresponds to the sensori-motor area, and also around the calcarine fissure in the visual sphere. The association fibres are not myelinated. The fibres of the pyramidal efferent system have also no myelin. M.O., medulla oblongata; P.V., pons Varolii; O.M.N., oculo-motor nerve; O.C., optic commissure; F.A.C., frontal association centre; C.C., corpus callosum; C.F., central fissure, or fissure of Rolando; P.A.C., posterior association centre; V.S., visual sphere; C., cerebellum; S.C., spinal cord.

Flechsig considers that at least two-thirds of the cortex consists of neurons of association, and further that these association centres possess no neurons of the efferent or afferent projection systems. The last part of this statement is probably not correct, and has not been accepted in its entirety by the majority of neurologists.

Ambronn and Held confirm Flechsig in finding that the afferent fibres are myelinated before the efferent, in the central nervous system, but in the case of the nerve-roots this is reversed, the anterior root fibres being myelinated before the posterior.

Held has also demonstrated the important influence of stimulus on myelination. His experiments were made on cats, dogs, and rabbits, which are born blind. If light is admitted to one eye by opening the lid, more obvious myelination is found in the corresponding optic nerve, than in that of the opposite side. This is not due to the irritation caused by forcibly opening the lid, for if the lid be opened and the animal kept in the dark, no difference in the myelination of the two optic nerves is observable. Flechsig also showed that a child born at 8 months had more marked myelination of its optic nerves, a month later, than a child born in the usual way at the ninth month.

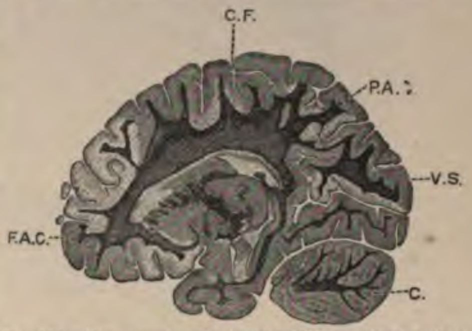

FIG. 502.—Diagram of vertical section of the brain of a child 5 months of age. The greater part of the white matter now shows myelination, thus indicating development of the association centres. The letters have the same meaning as in Fig. 688. (After Flechsig; Weigert method of staining.)

The richness of the brain in myelinated fibres increases for many years after birth with the progress of intellectual development. Kaes states this continues up to forty years of age, and that in old age the number diminishes. Myelin appears to be necessary for the functional activity of nerve tracts, and its development progresses *pari passu* with development of function; the reverse change (atrophy and degeneration) is correspondingly accompanied with marked disturbances of function.

Association Fibres and Association Centres.

We know by common experience that any group of muscles can be voluntarily contracted in reply to any form of stimulus, cutaneous, visual, auditory, etc. If, for instance, the wrist is flexed in response to an auditory stimulus, the nerve impulses pass first to the auditory area, then by certain fibres to the cerebral cells which control the muscles of the arm. The fibres which connect the two areas are termed *association fibres*. A diagrammatic view of the principal bundles of association fibres is given in fig. 503. This figure may be usefully compared with the next (fig. 504), which shows the general plan of the projection fibres.

The term "*association centres*" is given by Flechsig to those portions of the cortex that lie between the sensory centres he has been able to demonstrate. The function of these centres is first to furnish pathways between the several centres, and second to retain as memories previous sense impressions, so that in action they may modify the impulses sent into them, and by these modifications adjust to an almost infinite degree the form of the final response.

The association centres comprise a very large area of the cortex, and are divided into three:—(1) The great anterior association centre in the frontal lobe; (2) the posterior association centre in the parieto-temporal region; (3) the middle association centre; this is smaller and coincides with the island of Reil. These regions are in fact those in which no evident response follows excitation; they are sometimes called the "latent or inexcitable cortex." The human brain is characterised by the high development of these parts, and as already explained they are doubtless, as Flechsig terms them, the organs of thought.

The importance of the association of ideas, which has for its anatomical basis the association of cortical centres, will be at once grasped when one considers such

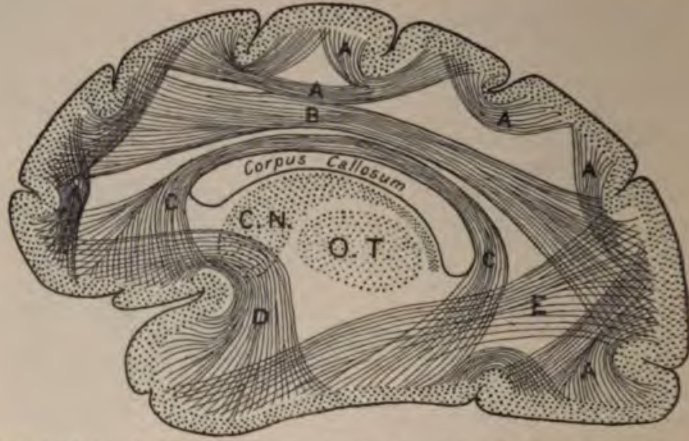

FIG. 503.—Lateral view of a human hemisphere, showing the main bundles of association fibres (Starr). A, A, between adjacent convolutions; B, between frontal and occipital areas; C, between frontal and temporal areas (cingulum); D, between frontal and temporal areas (fasciculus uncinatus); E, between occipital and temporal areas (fasciculus longitudinalis inferior); C.N., caudate nucleus O.T., optic thalamus.

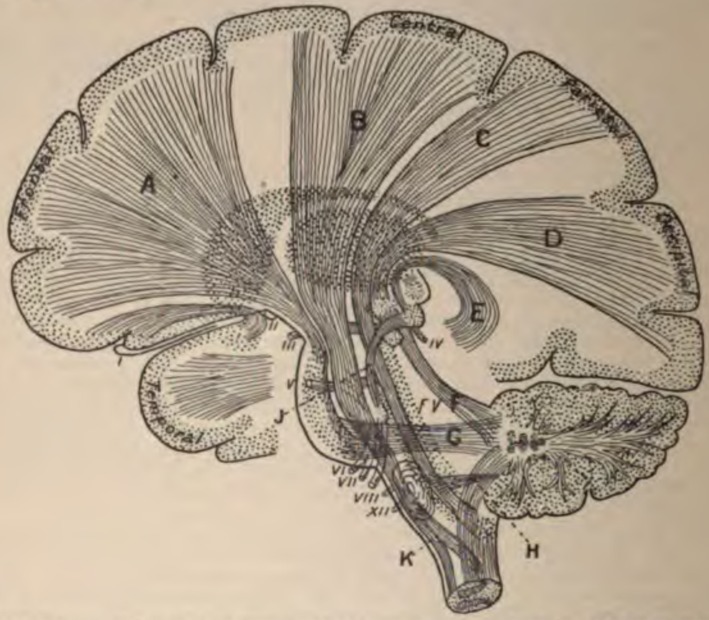

FIG. 504.—Schema of the projection fibres within the brain (Starr). A, tract from the frontal gyri to the pons nuclei and so to the cerebellum; B, motor pyramidal tract; C, sensory tract for touch (separated from B for the sake of clearness in the diagram); D, visual tract; E, auditory tract; F, G, H, superior, middle, and inferior cerebellar peduncles; J, fibres between the auditory nucleus and the inferior corpus quadrigeminum; K, motor decussation in the bulb; F.V., fourth ventricle. The numerals refer to the cranial nerves. The sensory radiations are seen to be massed towards the occipital end of the hemisphere.

complex actions as reading aloud or writing from dictation. The accompanying diagram (fig. 505) shows the position of the main centres involved, particulars of which will be found in the small text beneath the figure.

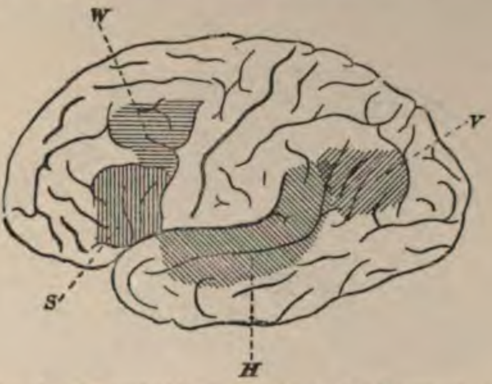

FIG. 505.—Lateral view of the left cerebral hemisphere of man (after Donaldson). V is the cortical area, damage to which produces "word blindness"; it is situated in the angular gyrus, and is called the *visual word centre*. H is the area in the superior temporal convolution, called the *auditory word centre*, damage to which produces "word deafness." S is Broca's convolution, damage to which produces loss of audible speech (motor aphasia); this is the sensori-motor area for the movements of the tongue, vocal cords, etc., concerned in speaking; Bastian terms it the *glosso-kinæsthetic area*. The area W, called by Bastian the *cheiro-kinæsthetic area*, is the corresponding region concerned in hand movements, damage to which abolishes the power of writing (agraphia).

In reading aloud, the impressions of the words enter by the eyes, reach that portion of the visual sphere known as the *visual word centre*, travel across to the *auditory word centre* by association fibres, where the memory of their sounds is revived; another tract of association fibres connects this to the sensori-motor areas in Broca's convolution called by Bastian the *glosso-kinæsthetic area*, whence motor impulses originate which finally reach the muscles concerned in pronouncing the words originally seen.

Writing from dictation is just as complex; the course of the impulses is by the auditory channels to the *auditory word centre*, then by association tracts to the *visual word centre*, where the shapes of the letters composing the words are revived; another association tract carries on the impulse to the sensori-motor area connected with the movements of the hand (Bastian's *cheiro-kinæsthetic area*) in the middle region of the Rolandic cortex, and finally the movement of writing is accomplished. The diverse symptoms exhibited by patients suffering from various forms of aphasia can be all explained by more or less extensive damage either to the centres themselves or to the association tracts which connect them.

The association fibres of the spinal cord are described on p. 618.

In the development of a neuron, four stages can be distinguished:—(1) Cells without processes; (2) the appearance of simple branches, the axon developing most rapidly; (3) the formation of collaterals; (4) the appearance of the medullary sheath. In the cerebral convolutions the fibres become myelinated in a strictly regular sequence; some convolutions have their fibres medullated three months before birth, while in others complete myelination has not occurred six months later. Fibres of equally great importance become medullated at the same time; those of primary importance first, and so on. In this way, myelogenetic cortical fields can be mapped out, which retain their contours for some time. Thirty-six of such fields were made out by Flechsig, and can be divided chronologically into three groups, *primary*, *intermediate*, and *terminal*.

The *primary* fields are darkly shaded in the accompanying diagrams (figs. 506 and 507).

They are 10 in number, and are those provided with myelinated fibres at birth; they contain the seats of the cortical representation of all the senses. To No. 1 is assigned the cutaneous and muscular sense; to No. 2 the sense of smell; to No. 4 that of vision; to No. 5 that of hearing. The functions of some of the primary areas had not been determined. The principal efferent projection tracts originate from the primary fields; thus the pyramidal tract starts from No. 1, but mainly from the ascending frontal convolution.* The sensory fibres connected with the skin and muscles terminate mainly in the ascending parietal convolution. The inferior fornix is connected with Nos. 2 and 3. The inner bundle of the pes springs from 1 b, 6, 12, 14 and 15; the origin of the outer bundle of the pes is doubtful. From the visual area (No. 4) a tract arises which passes mainly into the anterior corpus quadrigeminum; the auditory zone (No. 5), towards which a tract proceeds

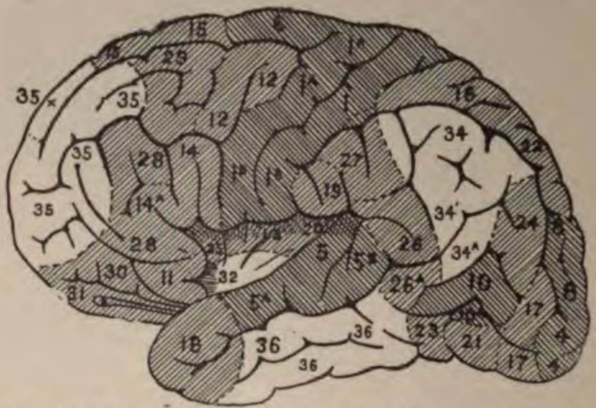

FIG. 506.—Outer surface of human brain, showing Flechsig's developmental zones; primary (1—10) darkly shaded; intermediate (11—31), less deeply shaded; terminal (32—36), not shaded. (Flechsig.)

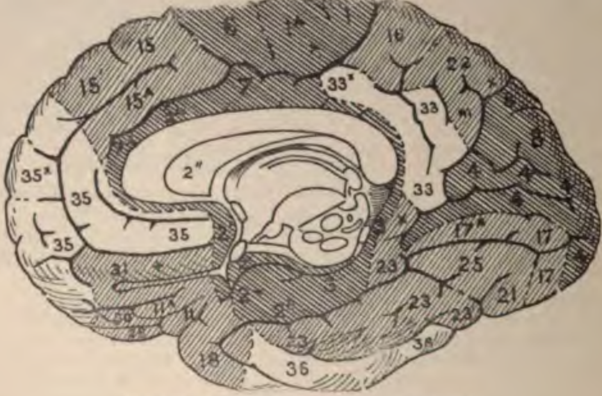

FIG. 507.—Inner surface of same. (Flechsig.)

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* This coincides well with the work of Sherrington and Grünbaum (p. 686).

that leads from the internal corpus geniculatum, sends an outgoing tract into the column of Türck, and thus motor functions of the upper part of the body are possible as a direct result of auditory impressions. In fact in every case each primordial sensory zone is connected with a well-defined pair of tracts, one proceeding to it (cortico-petal) and the other from it (cortico-fugal). It is thus impossible to speak of a purely motor or a purely sensory area.

The *terminal* areas (Nos. 31 to 36, unshaded in the diagrams) do not begin to be myelinated until at least a month after birth. These and the majority of the *intermediate* areas (Nos. 11 to 31, lightly shaded in the diagrams) show few or no projection fibres * even 8 months after birth. They comprise, in fact, the association centres, and are rich in long association fibres.

The view of Monakow, Déjerine, and others, that the fasciculus longitudinalis inferior (E in fig. 503, p. 694) and the cingulum (C in the same figure) are long association tracts is denied by Flechsig; they connect primordial zones, and are regarded by him as projection fibres, the former connecting the lateral corpus geniculatum with the cortical field of vision, and constituting the real optic radiation.

Electrical Variation in Central Nervous System.

Du Bois Reymond found that the spinal cord, like a nerve, exhibits a demarcation current between its longitudinal surface and a cross-section, and that a diminution of this current occurs on excitation (negative variation). Gotch and Horsley investigated the currents of the cord very thoroughly. If the Rolandic area of the cortex is stimulated, and a portion of the thoracic region of the spinal cord is led off to a galvanometer, a persistent negative variation followed by a series of intermittent variations is observed; this exactly corresponds to the tonic spasm followed by clonic contractions which occur in the muscles excited by this means.

The galvanometer in the hands of these observers also proved to be a valuable instrument for determining the paths taken by nervous impulses in the cord. One example will suffice: If the central end of one sciatic nerve is stimulated, the chief electrical variation in the cord is noticed to be obtained when the same side of the cord is led off to the galvanometer, but a certain amount of electrical variation is obtainable from the opposite side of the cord. This coincides with the fact ascertained by other methods, that the main sensory channel is on the same side of the cord as the entering nerves, but that there is a certain small amount of decussation below the level of the bulb.

Electromotive changes also occur during activity in the cortex cerebri, but they have not been much studied, and we do not know whether they have their seat in the grey or in the underlying white matter.

Sleep.

The conditions that favour sleep are:—

(1) A diminution of the impulses entering the central nervous system by the afferent channels. This is under our voluntary

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* That they never have any projection fibres at all is denied by most observers.

control, as, for instance, in closing the eyes, or retiring to a quiet room.

(2) Fatigue. This diminishes the readiness of the central nervous system to respond to stimuli.

The first two hours of sleep are always the most profound; later on, relatively weak stimuli will cause awakening. Of the parts of the central nervous system, the spinal cord is always less profoundly affected than the brain, but even the brain is never entirely irresponsive, and unless slumber is very profound, dreams are the subjective result of external stimuli.

Sleep has been attributed by some to changes in the blood-supply of the brain, and ultimately referred to fatigue of the vaso-motor centres. The existence of an effective vaso-motor mechanism in the cerebral blood-vessels themselves is problematical (see p. 312); so that if changes occur in the cerebral blood-pressure or rate of flow, they are mainly secondary to those which are produced in other parts of the body. Plethysmographic records from the arm of a sleeping man show a diminution in its volume every time he is disturbed, even though the disturbance may not be sufficient to awaken him. This is interpreted as meaning a diminution in the blood of the body, and a corresponding increase in the blood-flow through the brain. It is, however, quite possible that the vascular condition is rather the concomitant or consequence of sleep than its cause.

Some of the theories to account for sleep have been chemical. Thus certain observers have considered that sleep is the result of the action of chemical materials produced during waking hours, which have a soporific effect on the brain; according to this theory awakening from sleep is due to the action of certain other materials produced during rest, which have the opposite effect. Obersteiner has gone so far as to consider that the soporific substances are reducing in nature, and others regard them as alkaloidal. These theories all rest upon the slimsiest foundations, and none has yet been found to stand experimental tests.

Then there are what we may term histological theories of sleep, and these are equally unsatisfactory. The introduction of the Golgi method opened a fresh field for investigators, and several have sought to find by this method a condition of the neurons produced by narcotics like opium and chloroform, which is different from that which obtains in the waking state.

Demoor and others found that in animals in which deep anæsthesia has occurred, that the dendrites exhibit moniliform swellings, that is, a series of minute thickenings or varicosities. On the strength of this observation, he has formulated what we may call a bio-physical theory of sleep. In the waking state, the neighbouring nerve units are in contact with each other; transmission of nerve impulses from neuron to neuron is then possible, and the result is consciousness; during sleep the dendrites are retracted in an amœboid manner; the neurons are therefore separated, and the result is unconsciousness.

Lugaro, on the other hand, takes the precisely contrary view. He was not able to discover moniliform enlargements, and his biophysical hypothesis is that the interlacing of dendrites is much more intimate during sleep than during consciousness. He therefore explains sleep by supposing that the definite and limited relationships between neurons no longer exists, but are lost and rendered ineffective by the universality of the connecting paths. It is not very difficult to explain such divergence of views, for they both depend mainly on observations made by a single method; and the method itself is open to objection. It is one which gives even in the same brain most inconstant results, and is not calculated to show much more than a mere outline of a few of the cells and their branches. So much doubt has arisen of late in regard to the trustworthiness of the method, that many neurologists are beginning to doubt whether the neuron theory implying absolute non-continuity of nerve units has been satisfactorily proved, and there is a tendency to return to the idea of a connecting network not very different from that originally put forward by Gerlach.

A more satisfactory investigation of the effect of anæsthetics on nerve-cells was carried out by Hamilton Wright.

He used rabbits and dogs, and subjected them to ether and chloroform narcosis for periods varying from half an hour to nine hours. In both animals he found that the nerve-cells are affected, but in rabbits much more readily. This accords quite well with what is known regarding the susceptibility of rabbits as compared to dogs towards the influence of these narcotising agents. In a rabbit, the nerve-cells, especially of the cerebrum, show changes even after only half an hour's anæsthesia, but in dogs at least four hours' anæsthesia must be employed. By the Golgi method the moniliform enlargements can be seen. These become more numerous, larger, and encroach more and more on the dendritic stems, the longer the anæsthesia is kept up. The accompanying illustrations show the appearances seen (fig. 508).

Lugaro's failure to find these appearances is doubtless due to his not having maintained the anæsthesia long enough in his dogs.

Wright started his work with a bias in favour of Demoor's biophysical theory, but he soon found that the theory was untenable; the results of his observations have shown him that the action of anæsthetics is bio-chemical rather than bio-physical, and he has been led to this conclusion by the employment of other histological methods, particularly the most sensitive one we possess, namely, the methylene-blue reaction.

Owing to the chemical action of the anæsthetic on the cells, the Nissl bodies have no longer an affinity for methylene-blue, and the cells consequently present what Wright calls a rarefied appearance; when this becomes marked the cells appear like the skeletons of healthy cells. In extreme cases the cells look as though they had undergone a degenerative change, and after eight or nine hours' anæsthesia in dogs, even the nucleus and nucleolus lose their affinity for basic dyes. The change, however, is not a real degeneration, and passes off when the drug disappears from the circulation. Even after nine hours' anæsthesia the cells return rapidly to their normal condition, stain normally, moniliform enlargements have disappeared, and no nerve-fibres show a trace of Wallerian degeneration. The pseudo-degenerative change produced by the chemical action of the anæsthetic no doubt interferes with the normal metabolic activity of the cell-body, and this produces effects on the cell-branches. In the early stages of Wallerian degeneration, the branch of the nerve-cell which we call the axis-cylinder presents swellings or varicosities, produced by hydration or some similar chemical change. The moniliform enlargements seen during the temporary pseudo-degenerative effects produced by anæsthetics are comparable to this.* These

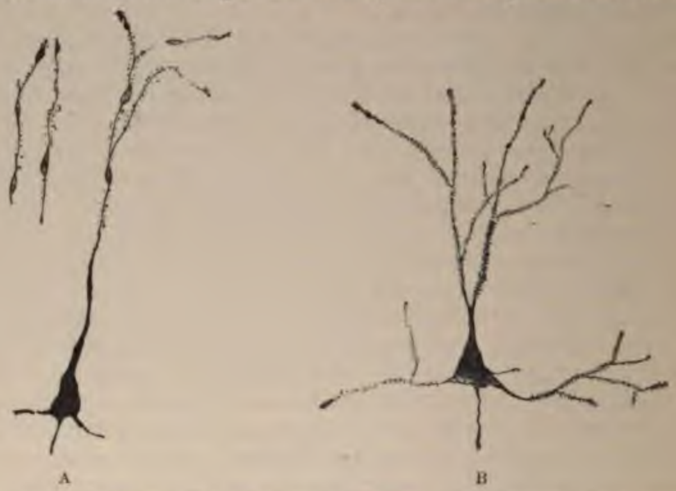

FIG. 508.—Moniliform enlargements on dendrites of nerve-cells, rendered evident by Cox's modification of Golgi's method. A, in a cortical cell of a rabbit; B, in a corresponding cell of a dog's brain, after six hours' anæsthetisation with ether in each case. (Hamilton Wright.)

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* Some observers look upon the varicosities as artifacts. If they are, they ought to have been found in all Wright's specimens, for the method of preparation was the same throughout.

enlargements are therefore not the primary cause of loss of consciousness, but are merely secondary results of changes in the cell-body. When a tree begins to wither the earliest apparent change is noticed in the branches most remote from the centre of nutrition, the root; as the changes in the centre of nutrition become more profound, the larger branches become implicated, but the seat of the mischief is not primarily in the branches. This illustration may serve to render intelligible what is found in nerve-cells and their branches.

Whether the appearances found in dogs and rabbits are applicable to the human subject is another question. I am inclined to think that we may safely regard them as such; there is no reason why an anæsthetic should act differently in different animals. The resistance of the animal is a variable factor, and this causes a variation in degree only; the effect is probably the same in kind for all animals, man included.

But I feel that we should be very chary in concluding that the artificial sleep of a deeply-narcotised animal is any criterion of what occurs during normal sleep. The sleep of anæsthesia is a pathological condition due to the action of a poison. The drug reduces the chemico-vital activities of the cells, and is, in a sense, dependent on an increasing condition of exhaustion, which may culminate in death. Normal sleep, on the other hand, is not produced by a poison, or at any rate we have no evidence of any poison; it is the normal manifestation of one stage in the rhythmical activity of nerve-cells, and though it may be preceded by fatigue or exhaustion, it is accompanied by repair, the constructive side of metabolic activity.

Loss of sleep is more damaging than starvation. Dogs will recover after being starved for three weeks, but they die from loss of sleep in five days. The body temperature falls, reflexes disappear, and *post-mortem* the brain is found to contain capillary hæmorrhages, the cord is dry and anæmic, and fatty degeneration is found in most of the tissues.

In man, loss of sleep curiously enough causes a slight rise in weight; the body temperature falls; the excretion of nitrogen and still more so that of phosphoric acid increases; the reactions of the muscular, and later those of the nervous, system diminish in intensity, except that in all cases there is an increase in acuteness of vision. These experiments were made by Patrick and Gilbert on three young men, who voluntarily went without sleep for ninety hours. At the end of the experiment a very small extra amount of sleep beyond the normal caused complete restoration, and all the symptoms, including the increase of weight, disappeared.

CHAPTER XLIX

FUNCTIONS OF THE CEREBELLUM

In past times there have been several views held as to the functions of the cerebellum. One of the oldest of these was the idea that the cerebellum was associated with the function of generation; another view, first promulgated by Willis, was that the cerebellum contained the centres which regulate the functions of organic life; this arose from the circumstance that diseases of the cerebellum are often associated with nausea and vomiting; it is a familiar fact that in displacements of equilibrium such as occur on board ship in a rough sea, or in the disease called Menière's disease, sickness is a frequent result; it appears from this that the cerebellum does receive from or send to the viscera certain impulses. The third and last of these older theories was that the cerebellum was the centre for sensation. This arose from the fact that certain of the afferent channels of the spinal cord were traced into the cerebellum. The impulses that travel along these, however, though afferent, are not truly sensory, and their reception in the cerebellum is not associated with consciousness.

The true function of the cerebellum was first pointed out by Flourens, and our knowledge about it has not advanced much from the condition in which Flourens left it. He showed that the cerebellum is the great centre for the co-ordination of muscular movement, and especially for that variety of co-ordination which is called equilibration—that is, the harmonious adjustment of the working of the muscles which maintain the body in a position of equilibrium.

It must not be supposed from this that the cerebellum is the sole centre for co-ordination. We have already seen that all the machinery necessary for carrying out very complicated locomotive movements is present in the spinal cord. The higher centres set this machinery going, and the work of arranging what muscles are to act, and in what order, is carried out by the whole of the grey matter from the corpora striata to the end of the spinal cord, including such outgrowths as the corpora quadrigemina and cerebellum. An instance of a complex co-ordinated movement is seen in what we learnt to call in the last chapter *conjugate deviation of head and eyes.* The higher cortical centre gives the general word of command to turn the head and eyes to the right: the subsidiary centres or subordinate officials arrange that this is to be accomplished by the external rectus of the right eye supplied by the right sixth nerve, the internal rectus of the left eye supplied by the left third nerve, and numerous muscles of neck and back of both sides supplied by numerous nerves. We thus see how the complicated intercrossing of fibres and connections of the centres of the various nerves are brought into play.

The functions of the cerebellum are investigated by the same two methods of experiment (*stimulation* and *extirpation*) that are employed in similar researches on the cerebrum. The anatomical connections of the cerebellum with other parts of the cerebro-spinal axis (see p. 651) have been chiefly elucidated by the degeneration method. Each side of the cerebellum has three peduncles: the *superior* peduncle connecting it to the opposite hemisphere of the cerebrum, the *inferior* peduncle connecting it mainly to the same side of the spinal cord, and the *middle* peduncle contains fibres which link the two halves of the cerebellum together in a physiological though not in an anatomical sense. The upper end of the inferior peduncle terminates in the vermis; in some of the lower animals the vermis is practically the only part of the cerebellum which is present, and it is this part of the cerebellum which is principally concerned in the co-ordination of the bodily movements. The cerebellar hemispheres are especially connected with the opposite cerebral hemispheres; and possibly just as the different regions of the body have corresponding areas in the cerebrum, so also they are similarly represented in the cerebellum; but localisation of function in the cerebellum has not gone sufficiently far yet to make this a certainty.

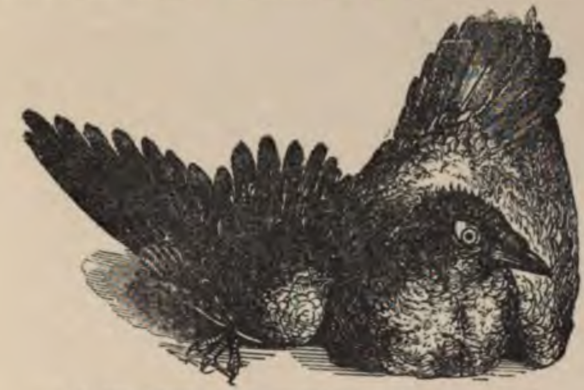

FIG. 509.—Pigeon after removal of the cerebellum. (Dalton.)

If the cerebellum is removed in an animal, or if it is the seat of disease in man, the result is a condition of slight muscular weakness; but the principal symptom observed is *inco-ordination*, chiefly evidenced by a staggering gait similar to that seen in a drunken man. It is called *cerebellar ataxy.*

This condition is well illustrated in the figure on p. 703 (fig. 509); the disturbed condition of the animal contrasts very forcibly with the sleepy state producèd by removal of the cerebrum (see fig. 492).

In order that the cerebellum may duly execute its function of equilibration, it is necessary that it should send out impulses; this it does by fibres that leave its cells and pass out through its peduncles; they pass out to the opposite cerebral hemisphere, and so influence the discharge of the impulses from the cortex of the cerebrum. It is also probable that impulses pass out to the cord (see dotted line in fig. 482), but the exact course of these fibres, if they do exist, has still to be worked out.

The cerebellum thus acts upon the muscles of the same side of the body in conjunction with the cerebral hemisphere of the opposite side. The close inter-relation of one cerebral with the opposite cerebellar hemisphere is shown in cases of brain disease, in which atrophy of one cerebellar hemisphere follows that of the opposite cerebral hemisphere (see fig. 510).

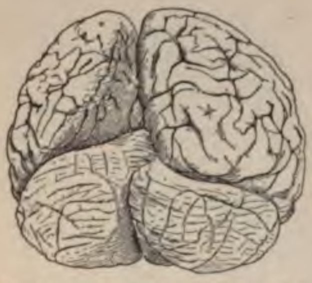

FIG. 510.—This is a reproduction of a photograph of a lunatic's brain lent me by Dr Fricke. One cerebral and the opposite cerebellar hemisphere are atrophied.

In order that the cerebellum may send out impulses in this way, it is necessary that it receive impulses which guide it by keeping it informed of the position of the body in space. These afferent impulses are of four kinds, namely:—

1. Tactile.
2. Muscular.
3. Visual.
4. Labyrinthine.

We will take these one by one:—

1. *Tactile impressions.*—The importance of impulses from the skin is shown in those diseases of the sensory tracts (especially locomotor ataxy) where there is diminution in the tactile sense in the soles of the feet. In such cases the patient cannot balance himself while standing with his eyes shut. The same effect may be produced experimentally by freezing the soles of the feet.

Again, if the skin is stripped from the hind limbs of a brainless frog, it is unable to execute such reflex actions as climbing an inclined plane, which it can do quite well when the skin is uninjured.

2. *Muscular impressions.*—Quite as important as the tactile sense from the skin is the muscular sense, the sense which enables us to know what we are doing with our muscles. We have hitherto chiefly spoken of the muscular nerves as being motor; they also contain sensory fibres; these pass from the muscles, and their tendons to the posterior roots of the spinal nerves, and the impulses ascend the sensory tracts through cord and brain to reach the cerebellum and the Rolandic area. In some cases of locomotor ataxy there is but little loss of tactile sensibility, and the condition of inco-ordination is then chiefly due to the loss of the muscular sense.

3. *Visual impressions.*—The use of visual impressions in guiding the nervous centres for the maintenance of equilibrium is seen in those cases of locomotor ataxy where there is loss of equilibrium when the patient closes his eyes. Destruction of the eyes in animals often causes them to spin round and lose their balance. The giddiness experienced by many people on looking at moving water, or after the onset of a squint, or when objects are viewed under unusual circumstances, as in the ascent of a mountain railway, is due to the same thing. The importance of keeping one's eyes open is brought home to one very forcibly when one is walking in a perilous position, as along the edge of a precipice, where an upset of the equilibrium would be attended with serious consequences.

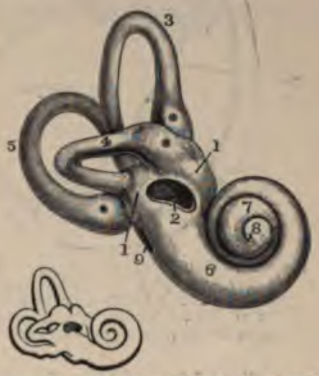

Fig. 511.—Right bony labyrinth, viewed from the outer side. The specimen here represented was prepared by separating piecemeal the looser substance of the petrous bone from the dense walls which immediately enclose the labyrinth. 1, the vestibule; 2, fenestra ovalis; 3, superior semicircular canal; 4, horizontal or external canal; 5, posterior canal; *, ampullæ of the semicircular canals; 6, first turn of the cochlea; 7, second turn; 8, apex; 9, fenestra rotunda. The smaller figure in outline below shows the natural size. (Sömmering.)

4. *Labyrinthine impressions.*—These are the most important of all; they are the impressions that reach the central nervous system from that part of the internal ear called the labyrinth. Here, however, we must pause to consider first some anatomical facts in connection with the semicircular canals that make up the labyrinth. Fig. 511 is an external view of the internal ear; it is enclosed within the petrous portion of the temporal bone; and consists of three parts—the vestibule (1), the three semicircular canals (3, 4, 5) which open into the vestibule, and the tube, coiled like a snail's shell, called the cochlea (6, 7, 8). The cochlea is the part of the apparatus which is concerned in the reception of auditory impressions; it is supplied by the cochlear division of the eighth or auditory nerve. The

remainder of the internal ear is concerned not in hearing, but in the reception of the impressions we are now studying. Within the vestibule are two chambers made of membrane, called the utricle and the saccule; these communicate with one another and with the canal of the cochlea. Within each bony semicircular canal is a membranous semicircular canal of similar shape. Each canal is filled with a watery fluid called *endolymph*, and separated from the bony canal by another fluid called *perilymph*. Each canal has a swelling at one end called the ampulla. The membranous canals open into the utricle; the *horizontal* canal by each of its ends; the *superior* and *posterior* vertical canals by three openings, these two canals being connected at their non-ampullary ends.

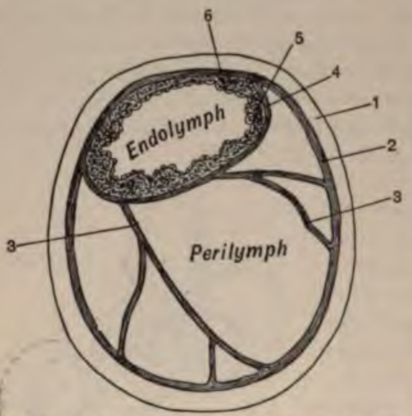

FIG. 512.—Section of human semicircular canal. (After Rüdinger.) 1, Bone; 2, periosteum; 3, 3, fibrous bands connecting the periosteum to 4, the outer fibrous coat of the membranous canal; 5, tunica propria; 6, epithelium.

Fig. 512 shows in transverse section the way in which the membranous is contained within the bony canal; the membranous canal consists of three layers, the outer of which is fibrous and continuous with the periosteum that lines the bony canal; then comes the *tunica propria*, composed of homogeneous material, and thrown into papillæ except just where the attachment of the membranous to

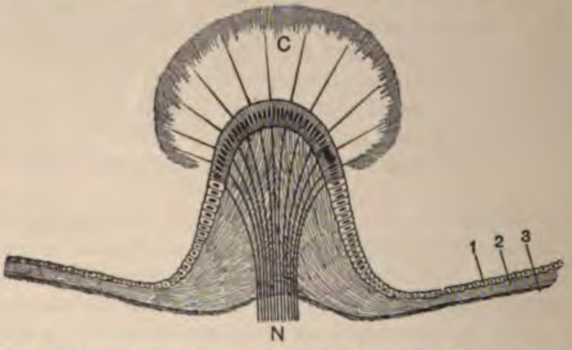

FIG. 513.—Section through the wall of the ampulla of a semicircular canal, passing through the crista acoustica. 1, Epithelium; 2, tunica propria; 3, fibrous layer of canal; N, bundles of nerve-fibres; C, cupula, into which the hairs of the hair-cells project. (After Schäfer).

the bony canal is closest; and the innermost layer is a somewhat flattened epithelium.

At the ampulla there is a different appearance; the tunica propria is raised into a hillock called the *crista acoustica* (see fig. 513); the cells of the epithelium become columnar in shape, and to some of them fibres of the auditory nerve pass, arborising round them; these cells are provided with stiff hairs, which project into what is called the *cupula*, a mass of mucus-like material containing otoliths or crystals of calcium carbonate. Between the hair-cells are fibre-cells which act as supports (fig. 514). When the endolymph in the interior of the canals is thrown into vibration, the hairs of the hair-cells are affected, and a nervous impulse is set up in the contiguous nerve-fibres, which carry it to the central nervous system.

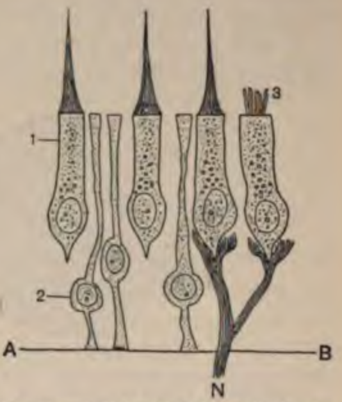

FIG. 514.—1, Hair-cell; 3, hair-cell, showing the hair broken, and the base of the hair split into its constituent fibrils; 2, fibre-cell; N, bundle of nerve-fibres which have lost their medullary sheath, and terminate by arborising round the base of the hair-cells; A.B., surface of tunica propria. (After Retzius).

The walls of the saccule and utricle are similar in composition, and each has a similar hillock, called a *macula*, to the hair-cells on which nerve-fibres are distributed.

The macula of the utricle and the cristæ of the superior and horizontal canals are supplied by the vestibular division of the eighth or auditory nerve. The macula of the saccule and the crista of the posterior canal are supplied by a branch of the cochlear division of the same nerve (see p. 643).

When these canals are diseased in man, as in Menière's disease, there are disturbances of equilibrium: a feeling of giddiness, which may lead to the patient's falling down, is associated with nausea and vomiting. In animals similar results are produced by injury, and the subject has been chiefly worked out on birds by Flourens, where the canals are large and readily exposed, and more recently in fishes, by Lee.

Thus, if the horizontal canal is divided in a pigeon, the head is thrown into a series of oscillations in a horizontal plane, which are increased by section of the corresponding canal of the opposite side. After section of the vertical canals, the forced movements are in a vertical plane, and the animal tends to turn somersaults.

"When the whole of the canals are destroyed on both sides the disturbances of equilibrium are of the most pronounced character. Goltz describes a pigeon so treated which always kept its head with the occiput touching the breast, the vertex directed downwards, with the right eye looking to the left and the left looking to the right, the head being incessantly swung in a pendulum-like manner. Cyon says it is almost impossible to give an idea of the perpetual movements to which the animal is subject. It can neither stand, nor lie still, nor fly, nor maintain any fixed attitude. It executes violent somersaults, now forwards, now backwards, rolls round and round, or springs in the air and falls back to recommence anew. It is necessary to envelop the animals in some soft covering to prevent them dashing themselves to pieces by the violence of their movements, and even then not always with success. The extreme agitation is manifest only during the first few days following the operation, and the animal may then be set free without danger; but it is still unable to stand or walk, and tumultuous movements come on from the slightest disturbance. But after the lapse of a fortnight it is able to maintain its upright position. At this stage it resembles an animal painfully learning to stand and walk. In this it relies mainly on its vision, and it is only necessary to cover the eyes with a hood to dispel all the fruits of this new education, and cause the reappearance of all the motor disorders." (Ferrier.)

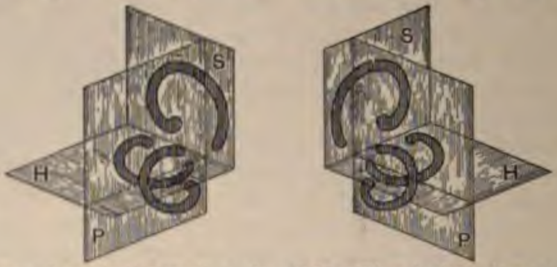

Fig. 515.—Diagram of semicircular canals, to show their positions in three planes at right angles to each other. It will be seen that the two horizontal canals (H) lie in the same plane: and that the superior vertical of one side (S) lies in a plane parallel to that of the posterior vertical (P) of the other. (After Ewald.)

It is these canals which enable all of us to know in which direction we are being moved, even though our eyes are bandaged, and the feet are not allowed to touch the ground. On being whirled round, such a person knows in which direction he is being moved, and feels that he is moving so long as the rate of rotation varies, but when the whirling stops he seems, especially if he opens his eyes, to be whirling in the opposite direction, owing to the rebound of the fluid in the canals. The forced movements just described in animals are due both to the absence of the normal sensations from the canals and to delusive sensations arising from their irritation, and the animal makes efforts to correct the movement which it imagines it is being subjected to.

Artificial stimulation of the canals produces movements of the head and orbits, and giddiness. Similar movements occur during bodily rotation, and giddiness is the result of a rivalry of sensations which afford conflicting ideas of the position of the body relatively to external objects. A certain proportion of deaf mutes lose their sense of direction under water, cannot maintain their equilibrium when their eyes are shut, exhibit no orbital movements when rotated, and never suffer from sea-sickness or giddiness. This proportion (36 per cent.) is approximately the frequency in which abnormal conditions of the canals have been found *post-mortem* in deaf mutes.

It will be noticed that the canals of each side are in three planes at right angles to each other, and we learn the movements of our body with regard to the three dimensions of space by means of impressions from the ampullary endings of the auditory nerve; these impressions are set up by the varying pressure of the endolymph in the ampullæ.

Thus a sudden turning of the head from right to left will cause movement of the endolymph towards, and therefore increased pressure on, the ampullary nerve-endings of the left horizontal canal, and diminished pressure on the corresponding nerve-endings of the right side. It is probable that resulting from such a movement two impulses reach the brain, one the effect of increased pressure in one ampulla, the second the effect of decreased pressure in its fellow.

"One canal can be affected by, and transmit the sensation of rotation about one axis in one direction only; and for complete perception of rotation in any direction about any axis, six canals are required in three pairs, each pair being in the same or parallel planes, and their ampullæ turned opposite ways. Each pair would thus be sensitive to any rotation about a line at right angles to its plane or planes, the one canal being influenced by rotation in one direction, the other by rotation in the opposite direction." (Crum-Brown.)

The two horizontal canals are in the same plane; the posterior vertical of one side is in a plane parallel to that of the superior vertical of the other side (see fig. 515).

These four sets of impressions (tactile, muscular, visual, and labyrinthine) reach the cerebellum by its peduncles; from the eyes through the superior peduncle, from the semicircular canals through the middle and inferior peduncles, and from the body generally through the restiform body or inferior peduncle. Section and stimulation of the peduncles cause inco-ordination, chiefly evidenced by rotatory and circus movements similar to those that occur when the nerve-endings in the semicircular canals are destroyed or stimulated. Stimulation of the cerebellum itself—and this has been done through the skull in man—causes giddiness, and consequent muscular efforts to correct it. The results of stimulation, indeed, are precisely analogous to those of extirpation, only in the reverse direction. Loss of muscular tone which follows extirpation of the canals is probably the result of secondary changes in the brain.

CHAPTER L

COMPARATIVE PHYSIOLOGY OF THE BRAIN

It will have been noticed in the preceding chapters how much of our knowledge of cerebral functions is derived from observations and experiments performed upon the lower animals. I propose in this chapter to expand this part of the subject. It is important not only because of its intrinsic interest, but also because a wider survey of the conditions in various animals throws considerable light on what is found in man.*

The brain in the lower vertebrata is composed of a smaller number of cells than is found in the human brain; one notices also that the massing of the nerve units towards the cerebral cortex and in relation to the principal sense organs has gone on to a less extent.

The doctrine of cerebral localisation is not accurately expressed by the statement that a cortical centre is one, the stimulation of which produces a definite response, and the extirpation of which abolishes the response. We have, for instance, seen that the stimulation of certain areas in the dog's brain produces certain movements, but Goltz showed that in his dogs, the removal of an entire hemisphere did not cause paralysis of the opposite side of the body.

In the central nervous system there are few or no places, where only one set of nerve units are situated, with fibres passing to and from them. Almost every locality has several connections with other parts, and also fibres passing through it which connect together the parts on all sides of it. Hence in extirpating even a limited area, numerous pathways are interrupted, and the damage is consequently widespread. Much of the disturbance produced at first gradually passes away, and the *temporary* effects must be distinguished from those which are *permanent;* the permanent effects have the greater significance of the two. Moreover, it is clear that the relative and absolute value of any locality in the central nervous system depends largely on the degree to which centralisation has progressed, and on the amount of connection between the various areas. The closer the connection, the more numerous and intricate the pathways, the greater will be the permanent effects of an extirpation, and the recovery of function the more remote. The lower the animal in the zoological series, or the less the age of the animal, the more imperfectly developed will be the connecting strands, and so the possibility of other parts taking up to some extent the functions of those that are removed will be increased.

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* This subject is treated at some length in Dr Donaldson's article on the Central Nervous System in the American Text-book of Physiology edited by Howell. I am indebted to this article for much contained in the present chapter.

If the cerebral hemispheres are removed in a teleostean or bony fish (and in such animals there is practically no cortex), the animal is to all intents and purposes unaffected; it can distinguish between a worm and a piece of string, and will rise to red wafers in preference to those of another colour. The operation does not damage the primary centres of vision, and in these fishes the eye is the most important sense organ.

A shark, however, subjected to the same operation, is reduced to a condition of complete quiescence; this is due to the circumstance that in this fish the principal sense organ is that of smell, and severance of both olfactory tracts produces the same result as removal of the entire hemispheres. In either case the path between the olfactory bulbs and the centres that control the cord are interrupted.

Going a little higher in the animal scale to the frog, we find that removal of the hemispheres only does not entirely abolish its apparent spontaneity; it still continues to feed itself, for instance, by catching passing insects. It is not until the optic thalami are removed also that it becomes the purely reflex animal described on p. 678.

If the brain and the anterior end of the bulb are removed the frog becomes incessantly active, creeping and clambering about the room; but if the whole bulb is removed strong stimulation is required to produce movements; these, however, remain co-ordinated.

If the frog's cerebellum is removed there is some tremor of the leg muscles, and a loss of co-ordination in jumping. If the removal is confined to one side of the twixt-brain, mid-brain, or bulb, there is a tendency to forced positions and movements, action being most vigorous on the side of the body associated with the uninjured portions.

We thus see that a progressive removal of portions of the brain is followed by a progressive loss of responsiveness, until we reach the anterior end of the bulb, the removal of which sets free the lower centres of the cord, and the result is incessant movement provoked by slight stimuli. Further removal, however, lessens responsiveness, and this is not easy to explain.

In the bird, removal of the hemispheres and basal ganglia produces the sleepy condition already described (p. 679); when the animal is made to fly its movements are directed by the sense of sight, and it will select a perch to settle on in preference to the floor. It will start at a noise; it will not eat voluntarily; it exhibits no emotions such as fear, sexual feeling, or maternal instincts.

In mammals, the difficulty of the operation has been overcome by Goltz in dogs by removing the cerebrum piecemeal. One dog treated in this way lived in good health for eighteen months, when it was killed in order that a thorough examination of the brain might be made. It was then found that not only the hemispheres but the main parts of the optic thalamus and corpus striatum had been removed also. Though it could still carry out co-ordinated movements, its reactions were entirely reflex, and emotions, feelings, or the capacity to learn were entirely absent.

If we now compare these effects, it is seen that the results of the operation becomes progressively greater as we ascend the scale. The higher the animal, the more fatal the effects, the immediate disturbance more severe, the return of function slower, and the permanent loss greater. The long life of Goltz's dog was doubtless due to the fact that the removal was accomplished by several operations.

The higher animal loses just those characters which distinguish it from the lower ones. It is difficult to prophesy what would happen if as extensive operations were carried out in a monkey or a man. But so far as extirpation has been observed, the initial paralysis (which is seen also in the dog) does not disappear so rapidly or so completely. In man, the tendency to recover is least.

This is anatomically explicable when we remember that the anterior horn cells are influenced chiefly by two sets of impulses, those which enter the cord by the posterior roots, and those which come down from the cerebrum by the pyramidal tracts. In the lower animals the pyramidal pathway is insignificant, and when it is interrupted the disturbance is consequently slight. In animals below the mammals it is absent, and going up the mammalian scale it becomes more and more important as the following figures show:—

In the	mouse	the pyramidal fibres	constitute	1·14	per cent.	of those in the cord.
,,	guinea-pig	,,	,,	3·0	,,	,,
,,	rabbit	,,	,,	5·3	,,	,,
,,	cat	,,	,,	7·76	,,	,,
,,	man	,,	,,	11·87	,,	,,

We can therefore quite readily understand that in the apes and in man, a damage to the cortex which causes degeneration of these tracts will cut off many impulses to the anterior cornual cells, and produce a greater or less degree of paralysis.

We have already pointed out (p. 686) that the size of the cortical areas does not vary with the mere mass of the muscles under control, but with the increasing complexity and delicacy of the movement; (compare in fig. 498 the relative size of the areas which control the trunk muscles and the finger movements). It is just these movements which are most affected by a cortical injury, and which exhibit least recovery; in the upper limb, for instance, the shoulder muscles will be the least, and the hand the most, paralysed.

On the sensory side of the cortex, vision alone can be analysed with sufficient accuracy. The lower the animal in the series, the more readily can its actions be controlled by sensory impulses which have not passed through the cortex cerebri. A decerebrated bony fish can distinguish colours, a frog can catch flies, even a pigeon will select its perch, though it takes no notice of food or of people who try to frighten it. A dog similarly operated on is practically blind, though it will blink at a bright flash of light. In the lower animals the impulses pass in to the primary visual centre which acts as the centre for the reflex; the higher we ascend the animal scale, the path *viâ* the cortex becomes more permeable, of greater value or even indispensable, and the reflexes through the lower centres of less importance; not only so, but there are subdivisions of the visual cortical area, which correspond to different regions of the retinæ.

In the fishes which have no cortex cerebi, the optic lobes, analogous to the C. quadrigemina, are the centres for vision. In some fishes, a small number of the fibres of the optic nerve pass into the geniculate body, which forms a cell station on the road to the posterior region of the cerebrum, where a primitive cortex begins to appear. On ascending the animal scale, this group of fibres becomes more and more abundant, and this part of the cortex becomes more elaborate in structure. When we reach the monkeys, this part of the brain is cut off from the rest to form a distinct occipital lobe by the parieto-occipital fissure, which is frequently called the Affenspalte (ape's split). At first this lobe is smooth (fig. 497, p. 685), but as the great parietal association centres get larger with increase of intelligence, the visuo-sensory area is pushed back, and is thus thrown into folds. In the highest apes, and in the lower races of mankind, a good deal of the visuo-sensory sphere is still seen on the external cerebral surface; but in the higher races, most is pushed round on to the mesial surface (area 4, figs. 506, 507, p. 696). This *calcarine area* is better named the *striate area*, because it is characterised by the white stripe called the line of Gennari (see p. 689).

Some animals have *panoramic* and others *stereoscopic* vision. The former (mainly vegetable feeders) have eyes set laterally; each eye receives a different picture, and the decussation of the optic nerves is complete; each eye sends impulses to the opposite hemisphere. Animals with stereoscopic vision have the eyes, as in man, in front, and the optic axes can be converged so that an object is focussed with both eyes. This becomes necessary in carnivora, which have to catch moving prey; the more complex the movements of the fore-limb, the greater becomes the necessity for fixation of the eyes to guide them. In such animals each visual area corresponds with the same half of both retinæ, that is, with the opposite half of the visual field; the lower half of each area corresponds with the upper half of each half field of vision, and *vice versâ*. The appearance of the macula lutea (with cortical representation in both hemispheres) in the primates is the culminating point in visual development.

A man or an animal who loses both eyes is blind, but in time manages to find his way about. This is not the case when blindness is produced by removal or disease of both occipital lobes; here, the sense of orientation is lost also, for the association of many essential sensory and motor impulses is then impossible.

CHAPTER LI

SENSATION

BEFORE passing to the study of the various special senses, there are a number of general considerations in connection with the subject of sensation that demand our attention.

The psychologist divides the mental phenomena, which the physiologist localises in the brain, into three main categories:—

1. *Intellectual:* perceiving, remembering, reasoning, etc.
2. *Emotional:* joy, love, hate, anger, etc.
3. *Volitional:* purposing, deliberating, doing.

These are all closely connected together, and are all present in each healthy brain; but according as one or other may predominate, we speak of intellectual, emotional, or strong-willed individuals. The connection is especially close between intellect and will, which represent as it were the two sides of what we may call a conscious reflex action; the intellect gives the reason or stimulus for the exercise of the volitional power. The emotions are more complex, and we shall not discuss them; they are elaborate mental processes, in which sensations predominate.

The intellectual faculties are derived from the senses; sensations form the materials for intellect; in other words, we know and learn from what we see, feel, hear, taste, and smell. People born blind or deaf thus labour under the great disadvantage of having one or the other channel of knowledge closed; they can, however, make up for this in some measure by an education, and consequent increased sensitiveness of the channels that remain open.

The simplest mental operation is a **sensation**—that is, the conscious reception of an impression from the external world. For this the following things are necessary:—

1. A stimulus.
2. A nerve-ending to receive it.
3. A path to the brain.
4. A part of the brain to receive the impulse.

Partly through congenital, partly through acquired experience, the brain refers the sensation to the nerve-ending which received the stimulus; thus pain in the finger is referred to the finger, the sight of an object to the eyes, etc. If the ulnar nerve is stimulated by a knock on the elbow, the sensation is referred to the fingers where the nerve is distributed; if the stump of a recently amputated leg be stimulated, the brain not having got used to the new condition of things, refers the sensation to the toes, which still seem to be present.

Perception is a more complicated mental process; it consists in the grouping of sensations, and the imagining of the object from which they arise, and which is called the *percept.* The smell, the taste, the colour, etc., of an orange are all sensations; the grouping of these together constitutes the perception of an orange. Each mental process leaves an impress on the mind; these impressions build up memory, or *representative imagination;* this may be reproductive, as in recalling a friend's face; or constructive, as in picturing the face of an historical person.

During the whole operation, moreover, there must be *attention;* it is quite possible, for instance, in a dreamy person, that he may look at a thing without seeing it, or be present at a lecture without hearing it.

The more complex intellectual operations consist in the formation of *concepts,* and reasoning the grouping and discrimination of conceptions. Just as perception is built up of sensations, so **conception** is built up of perceptions. Thus the orange of our previous example is learnt to be one of similar substances called fruits; fruits to be products of the vegetable, as distinguished from the animal world, and so on.

This is seen in the education of a child: at first scattered sensations only are perceived, and by education he learns what these sensations correspond to in the external world, and how they may be classified. The other mental faculties are in the same way built of simpler material; from the first, perceptions and conceptions find an outlet in motor activity; at length the conscious realisation of ideas of movement culminate in the purposeful actions of **volition.** Moreover, every experience contains its own *quantum* of pain or pleasure, and produces reflex contractions or relaxations in vascular and other tissues, which in their turn possess a painful or pleasurable component. So, too, ideas acquire their colouring of pain or pleasure, ultimately elaborating the complex **emotions** of sorrow, joy, etc.

The nerve-endings that receive the impression from the external world are of various kinds. They may be simply ramifying and interlacing plexuses of nerve-fibrils, as in the cornea, parts of the skin, and in the interior of the body; this kind of nerve-ending is chiefly associated with *general sensibility*, that vague kind of sensation which cannot be put under any of the special headings—taste, sight, hearing, touch, and smell. The nerve-endings of the nerves of special sense are usually end-organs of a specialised kind. The most frequent kind of sensory end-organ is made of what is called *nerve-epithelium;* certain epithelial cells of the surface of the body become peculiarly modified, and grouped in special ways to receive the impressions from the outer world; these send an impulse into the arborisations at the termination of the axis-cylinders of the nerves which envelop the cells. One of these varieties of nerve-epithelium we have already made the acquaintance of, in the hair-cells of the semicircular canals; we shall find other kinds in the hair-cells of the cochlea, in the rods and cones of the retina, etc.

Pain is due to an excessive stimulation of the other sensory nerves, but there is some evidence that it may be a distinct sensation. Thus in some cases of diseases of sensory channels, tactile sensation may be intact, but sensitiveness to pain absent, and *vice versâ;* see also p. 668.

The other essential anatomical necessities for a sensation are the channels to the brain with their numerous cell-stations on the road, and the parts of the brain to which these tracts pass. Blindness, for instance, may not only be due to disease of the eye, but also to disease of the optic nerve, or of the parts of the brain to which the optic nerve passes.

A small stimulus, or a small increase or decrease in a big stimulus, will have no effect; a light touch, a feeble light, a gentle sound, may be so slight as to produce no effect on the brain. The smallest stimulus that produces an effect is called the *lower limit of excitation* or the *liminal* (from *limen*, a threshold) *intensity of the sensation.* The *height of sensibility* or *maximum of excitation* is a stimulus, so strong that the brain is incapable of recognising any increase in it; a bright light, for instance, may be so intense that any increase in its brightness is not perceptible. Between these two extremes we have what is called the *range of sensibility.* Most of our ordinary sensations fall somewhere about the middle of the range, and *Weber's law* (as expanded by *Fechner*) is a law that regulates the proportion between the stimulus and the sensation, and which is operative for this region of the range of sensibility. In general terms it may be stated that sensations increase as the logarithm of the stimuli; or, in order that the intensity of a sensation may increase in arithmetical progression, the stimulus must increase in a geometrical progression.

A definite example will help us to understand these mathematical terms a little better. We will select our example from the sense of vision, because the intensity of the cause of visual sensations, light, is easily measurable. Suppose a room lighted by 100 candles, and one candle more is brought in, the increase of light produced by the extra candle is quite perceptible to the eye; or if a candle were removed, the decrease in light would be perfectly appreciable. Next suppose the room lighted by 1000 candles, and one extra was brought in, no difference would be seen in the amount of illumination; in order to notice increase or decrease in the light it would be necessary to bring in ten extra candles, or take away ten of the candles, as the case might be. In each case an increment or decrease of one-hundredth of the original light is necessary to cause an increase or diminution in the sensation.

This is after all a perfectly familiar fact; a farthing rushlight will increase the illumination in a dimly-lighted cellar, but it makes no apparent difference in the bright sunshine.

The magnitude of the fraction representing the increment of stimulus necessary to produce an increase of sensation determines what is called the *discriminative sensibility.* This fraction differs considerably for different sense-organs; thus:—

For light it is $\frac{1}{100}$.

For weight it is $\frac{1}{40}$ to $\frac{1}{15}$ for different muscles.

For tactile pressure $\frac{1}{30}$ to $\frac{1}{10}$ in different parts of the body.

Another general consideration in connection with sensation is that the sensation lasts longer than the stimulus; a familiar instance of this is the sting after a blow. The *after-sensations,* as they are called, have been specially studied in connection with the eye (see After-images).

Subjective sensations are those which are not produced by stimuli in the external world, but arise in one's own inner consciousness; they are illustrated by the sensations experienced during sleep (dreams), and in the illusions to which mad and delirious people are subject.

Homologous stimuli.—Each kind of peripheral end-organ is specially suited to respond to a certain kind of stimulus. The homologous stimuli of the organs of special sense may be divided into:—

1. Vibrations set up at a distance without actual contact with the object; for instance, light and radiant heat.

2. Changes produced by actual contact with the object; for instance, in the production of sensations of taste, touch, weight, and alteration of temperature by conduction; in the case of the olfactory end-organs, the sensation is also excited by material particles given off by the odoriferous body, and borne by the air to the nostrils. In sound also, though there is no actual contact of the ear with the vibrating body which emits the sound, the organ of hearing is excited by waves of material substance, first of air, then of bones, then of endolymph, and these excite the nerve-endings of the internal ear.

When the eye is excited by any other kind of stimulus than by light, which is its adequate or homologous stimulus, the sensation experienced is light all the same; for instance, one sees sparks when the eyeball is struck; singing in the ears, the result of an accumulation of wax against the membrana tympani, is a similar example.

It has been inferred that there are separate nerve-fibres for the conveyance of each kind of sensation, and Johannes Müller expressed this idea in what is known as the law of *specific nerve energy*. He pointed out that the same nerve may be stimulated by mechanical or electrical means as well as in the normal physiological manner, and that in all cases the sensation—light, sound, taste, contact, etc., as the case might be—is the same. Hence it was argued that the psychical effect or sensation is independent of the nature of the stimulus, but dependent on the nature of the activity of the central cells among which the afferent fibres terminate. We have no observations which can decide whether the nerve impulses passing along the optic fibres are, for instance, similar to or different from those which are transmitted by the auditory fibres. The experiments of Langley and others on nerve-crossing (p. 173) would seem to indicate that the nervous impulse is an identical process in all nerves; and if this is so, we are obliged to infer that separate nerve-fibres convey the impulses destined to give rise to different sensations.

It is, however, possible that in the nerves of cutaneous sensation, the psychical process is determined by the nature of the peripheral stimulus, and consequently different branches of the same nerve-fibres may be imagined to be susceptible to different forms of stimulation, and thus two different sensations follow from the partial stimulation of the same nerve-fibres. Hering even argues in favour of the view that the nerve impulse has different characters in different afferent nerves, and further that it may be modified by the nature of the normal stimulus (*e.g.* in the skin, heat, cold, pain, or pressure). In the absence of direct experimental proof of such an idea, it is difficult to see upon what grounds it can rest.

CHAPTER LII

CUTANEOUS SENSATIONS

THE tactile end-organs are of numerous kinds, but the following are the principal ones :—

Pacinian Corpuscles.—These are named after their discoverer Pacini. They are little oval bodies, situated on some of the cerebro-spinal and sympathetic nerves, especially the cutaneous nerves of the hands and feet, where they lie deeply placed in the true skin. They also occur on the nerves of the mesentery of some animals like the cat. They have been observed also in the pancreas, lymphatic glands and thyroid glands, as well as in the penis. They are about $\frac{1}{12}$ inch long. Each corpuscle is attached by a narrow pedicle to the nerve on which it is situated, and is formed of several concentric sheaths of connective-tissue, each layer being lined by endothelium (figs. 517, 518); through its pedicle passes a single nerve-fibre, which loses its medullary sheath and enters a central core, at or near the distal end of which it terminates in an arborisation. Some of these layers are continuous with those of the perineurium, but some are super-added. In some cases two nerve-fibres have been seen entering one Pacinian body, and in others a nerve-fibre after passing unaltered through one has been observed to terminate in a second.

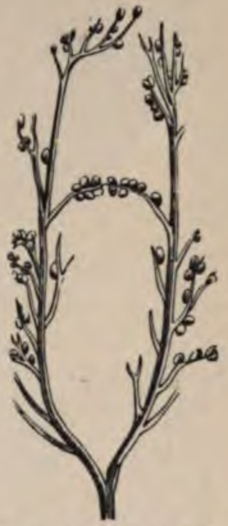

FIG. 516.—Extremities of a nerve of the finger with Pacinian corpuscles attached, about the natural size. (Adapted from Henle and Kölliker.)

The **corpuscles of Herbst** (fig. 519) are closely allied to Pacinian corpuscles, except that they are smaller and longer, with a row of nuclei around the central termination of the nerve in the core. They have been found chiefly in the tongues and bills of ducks.

End-bulbs are found in the conjunctiva (where in man they are spheroidal, but in most animals oblong), in the glans penis and clitoris, in the skin, in the lips, in the epineurium of nerve-trunks, and in tendon; each is about $\frac{1}{800}$ inch in diameter, oval or spheroidal, and is composed of a medullated nerve-fibre, which terminates among cells of various shapes. Its capsule contains a transparent or striated core, in the centre of which terminates the axis-cylinder of the nerve-fibre, the ending of which is somewhat clubbed (fig. 520).

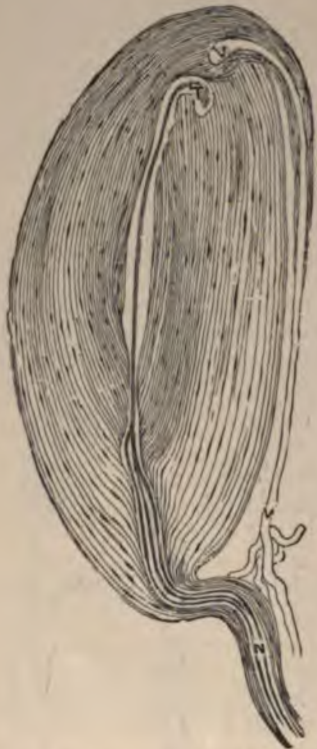

FIG. 517.—Pacinian corpuscle of the cat's mesentery. The stalk consists of a nerve-fibre (N) with its thick outer sheath. The peripheral capsules of the Pacinian corpuscle are continuous with the outer sheath of the stalk. The intermediary part becomes much narrower near the entrance of the axis-cylinder into the clear central core. A hook-shaped termination (T) is seen in the upper part. A blood-vessel (V) enters the Pacinian corpuscle, and approaches the end; it possesses a sheath which is the continuation of the peripheral capsules of the Pacinian corpuscle. ×100. (Klein and Noble Smith.)

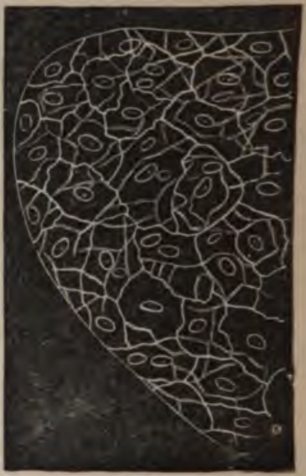

FIG. 518.—Summit of a Pacinian corpuscle of the human finger showing the endothelial membranes lining the capsules. × 220. (Klein and Noble Smith.)

Touch-corpuscles (Meissner's corpuscles), (figs. 521, 523), are found in the papillæ of the skin of the fingers and toes. They are small oblong masses, about $\frac{1}{200}$ inch long, and $\frac{1}{800}$ inch broad, composed of connective-tissue, surrounded by elastic fibres and a capsule of more or less numerous nucleated cells. They do not occur in all the papillæ of the parts where they are found, and, as a rule, in the papillæ in which they are present there are no blood-vessels.

The peculiar way in which the medullated nerve winds round and round the corpuscle before it enters it is shown in fig. 523. It loses its sheath before it enters into the interior, and then its axis-cylinder branches, and the branches after either a straight or convoluted course terminate within the corpuscle.

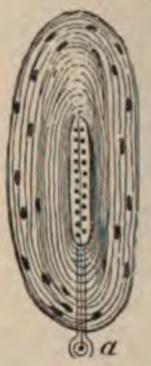

FIG. 519.—A corpuscle of Herbst, from the tongue of a duck. *a*, Medullated nerve cut away. (Klein.)

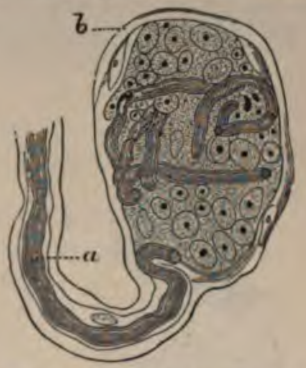

FIG. 520.—End-bulb of Krause. *a*, Medullated nerve-fibre; *b*, capsule of corpuscle.

The **corpuscles of Grandry** (fig. 522) form another variety, and have been noticed in the beaks and tongues of birds. They consist of oval or spherical cells, two or more of which compressed vertically

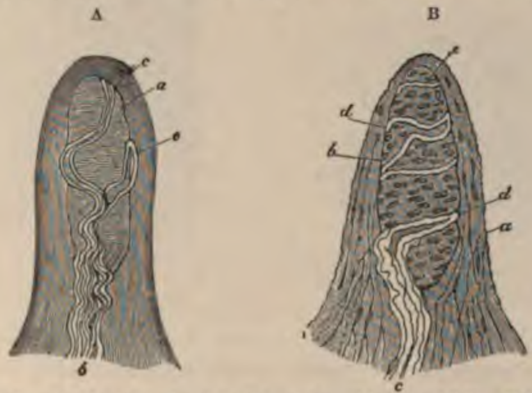

FIG. 521.—Papillæ from the skin of the hand, freed from the cuticle and exhibiting Meissner's corpuscles. A. Simple papilla with four nerve-fibres; *a*, tactile corpuscle; *b*, nerves with winding fibres *c* and *e*. B. Papilla treated with acetic acid; *a*, cortical layer with cells and fine elastic filaments; *b*, tactile corpuscle with transverse nuclei; *c*, entering nerve; *d* and *e*, nerve-fibres winding round the corpuscle. × 350. (Kölliker.)

are contained within a delicate nucleated sheath. The nerve enters on one side, and, laying aside its medullary sheath, terminates between the cells in flattened expansions.

Sensory nerve-endings in muscle.—Nerve terminations, sensory in function, are found in tendon. These appear very much like end-plates, and are represented in figs. 524 and 525. The *neuro-muscular spindles*, which are described on p. 86, are principally found in muscles in the neighbourhood of tendons and aponeuroses.

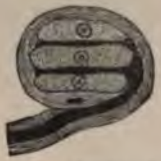

FIG. 522.—A corpuscle of Grandry, from the tongue of a duck.

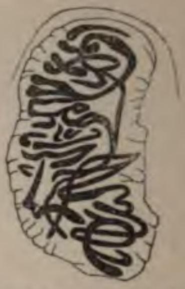

FIG. 523.—A touch-corpuscle from the skin of the human hand, stained with gold chloride.

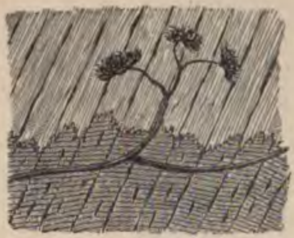

FIG. 524.—Termination of medullated nerve-fibres in tendon near the muscular insertion. (Golgi.)

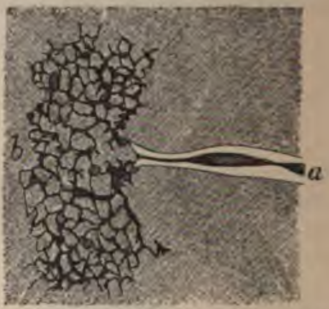

FIG. 525.—One of the reticulated end-plates of fig. 524, more highly magnified. *a*, Medullated nerve-fibre; *b*, reticulated end-plate. (Golgi.)

One of these spindles is shown in the accompanying drawing (fig. 526).

The principal grounds for believing the neuro-muscular spindles to be sensory are, first, that the nerve-fibres that supply them do not degenerate when the anterior roots of the spinal nerves are cut, and secondly, that they do degenerate when the posterior roots are divided (Sherrington). They also undergo degenerative changes in locomotor ataxy, which is a disease of the sensory nerve-units, and remain healthy in infantile paralysis, which is a disease of the motor cells of the anterior horn of the cord (Batten).

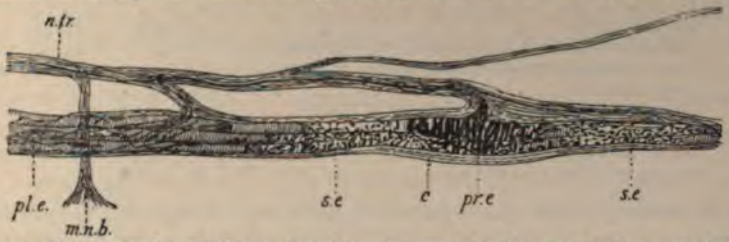

FIG. 526.—Neuro-muscular spindle. *c.*, Capsule; *n.tr.*, nerve trunk; *m.n.b.*, motor nerve bundle; *pl.e.*, plate-ending; *pr.e.*, primary nerve-ending; *s.e.*, secondary ending. (After Ruffini.)

In addition to the special end-organs, sensory fibres may terminate in **plexuses** of fibrils, as in the sub-epithelial and the intra-epithelial plexus of the cornea (fig. 527) and around the hair follicles in the skin generally. In some cases the nerve-fibrils within a stratified epithelium end in crescentic expansions (*tactile discs*) which are applied to the deeper epithelium cells. These are well seen in the skin of the pig's snout.

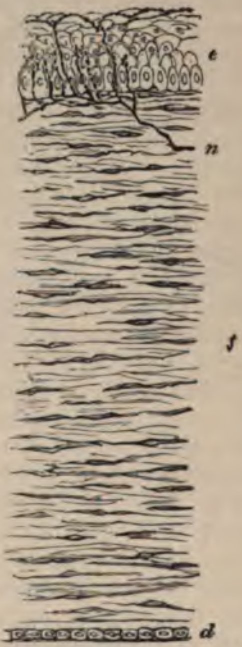

FIG. 527.—Vertical section of rabbit's cornea, stained with gold chloride. The nerves *n*, terminate in a plexus under and within the epithelial layer, *e*.

Localisation of Tactile Sensations.

The ability to localise tactile sensations on different parts of the surface is proportioned to the power which such parts possess of distinguishing and isolating the sensations produced by two points placed close together. This power depends in part on the number of nerve-fibres distributed to the part; for the fewer the fibres which any part receives, the more likely is it that several impressions on different contiguous points will act on only one nerve-fibre, and hence produce but one sensation. The experiments which have been made to determine the spatial relationships of the cutaneous sense consist in touching the skin, while the eyes are closed, with the points of a pair of compasses, and in ascertaining how close the points may be brought to each other, and still be felt as two points. (Weber). A few results are as follow:—

Tip of tongue	$\frac{1}{24}$-inch	1 mm.
Palmar surface of third phalanx of forefinger	$\frac{1}{12}$,,	2 ,,
Palmar surface of second phalanges of fingers	$\frac{1}{6}$,,	4 ,,
Palm of hand	$\frac{5}{12}$,,	10 ,,
Dorsal surface of first phalanges of fingers.	$\frac{7}{12}$,,	14 ,,
Back of hand	$1\frac{1}{6}$,,	25 ,,
Upper and lower parts of forearm	$1\frac{1}{2}$,,	37 ,,
Middle of thigh and back	$2\frac{1}{2}$,,	62 ,,

Moreover, in the case of the limbs, it was found that before they were recognised as two, the points of the compasses had to be *further* separated when the line joining them was in the long axis of the limb, than when in the transverse direction.

According to Weber the mind estimates the distance between two points by the number of unexcited nerve-endings which intervene between the two points touched. But the number of nerve-endings is not the only factor in the case. An important rôle is played by "local signature." Minute areas of the body surface have each their "local sign," *i.e.*, the sensation arising from stimulation of one area differs in some obscure quality from the sensations arising from stimulation of neighbouring areas, thereby acquiring its own spatial colouring which enables us to identify the area when stimulated. The difference of local sign between two near points may be imperceptible in one region of the body, but fully recognisable in another. Again, the delicacy of the sense of touch may be very much increased by practice. A familiar illustration occurs in the case of the blind, who, by constant practice, can acquire the power of reading raised letters, the forms of which are almost if not quite undistinguishable by the sense of touch to an ordinary person.

The power of correctly localising sensations of touch is gradually derived from experience. Thus, infants when in pain simply cry but make no effort to remove the cause of irritation, as an older child or adult would, on account of their imperfect knowledge of its exact situation. As education proceeds the brain gets to know more and more accurately the surface of the body, and the map of the surface in the brain is most accurately known where there is most practice of the sense of touch. The great delicacy of the tongue as a touch organ in judging the form and size of objects can be explained by the fact that this organ has to rely upon the sense of touch alone. Usually, in ascertaining the shape of an object or the part of the skin it touches, we use our eyes as well. In the case of the interior of the mouth this is impossible.

The different degrees of sensitiveness possessed by different parts may give rise to errors of judgment in estimating the distance between two points where the skin is touched. Thus, if the blunted points of a pair of compasses (maintained at a constant distance apart) are slowly drawn over the skin of the cheek towards the lips, it is almost impossible to resist the conclusion that the distance between the points is gradually increasing. When they reach the lips they seem to be considerably further apart than on the cheek. Thus, too, our estimate of the size of a cavity in a tooth is usually exaggerated when based upon sensation derived from the tongue alone. Another curious illusion is the following:—If we close the eyes, and place a marble between the crossed fore and middle fingers, we seem to be touching two marbles. This illusion is due to an error of judgment. The marble is touched by two surfaces which, under ordinary circumstances, could only be touched by two separate marbles; hence, the mind, taking no cognizance of the fact that the fingers are crossed, forms the conclusion that the two sensations are due to two marbles.

Varieties of Cutaneous Sensations.

The surface of the skin is a mosaic of tiny sensorial areas; but these areas are not set edge to edge as in the retina, but separated by relatively wide intervals which are not sensitive to stimuli just above liminal intensity. If the stimuli are made nearly minimal, the individual fields are reduced to small spots. Each of these spots subserves a specific sense, touch, cold, warmth or pain, and each doubtless coincides with the site of some special end organ, placed either singly or in clusters. The "touch spots," "cold spots," "warmth spots" and "pain spots" are intercommingled. In some districts one variety predominates, in others another. "Pain spots" are the most and "warmth spots" the least numerous. It is a matter of common experience that the sensitiveness of these varieties of cutaneous sensation differs in different parts of the body. The tip of the finger which is very sensitive to the true tactile sense (sense of pressure or contact) is not nearly so sensitive to alterations of temperature as the forearm or cheek to which a washerwoman generally holds her iron when forming a judgment of its temperature. Some parts of the skin are more sensitive to pain than others, and in the cornea we have an instance of a surface in which "pain spots" alone are present.

For the more accurate exploration of the skin *æsthesiometers* of various kinds have been invented. The sense of pressure may be estimated by the ability of the skin to distinguish different weights placed upon it; there must be no lifting of the weight, or the muscular sense is brought into play. The fraction which by Weber's law represents the discriminative sensibility (see p. 717) varies from $\frac{1}{30}$ to more than $\frac{1}{10}$ in different parts of the body. It does not, however, follow that the acuteness of the pressure sense varies exactly as the ability of accurately localising sensations; for instance, the skin of the forearm is as sensitive to pressure changes as that of the palm; and the tip of the tongue which is the most discriminative region of the body for locality is not so for pressure. For pressure stimuli which are near the limen or threshold of sensation, the hair æsthesiometer is much used; this is a hair or bristle mounted in a holder; the bristle can be shifted backwards or forwards in the holder, and the amount of pressure it exercises can thus be varied. It is used for the exploration of "touch spots," and these are found most numerously around the hair follicles. The touch spots are more numerous in some parts than in others, but fifteen for each square centimetre of skin is a rough average. To explore "pain spots" a mounted needle is used; in Griesbach's instrument the needle shifts up and down in the holder, and works against a spring which registers the amount of pressure exerted to evoke a painful sensation. In a "pain spot" the sensation is unaccompanied by "cold" or "warmth," even if a cold or warm needle is used. For the exploration of "heat spots" a small, hollow, metallic pencil is kept warm by a stream of warm water; this is moved over the surface; there are some points where the sensation is purely tactile, but at the "heat spots" the pencil will feel uncomfortably warm. "Cold spots" can be similarly mapped out by the use of a cold pencil. The accompanying figure (fig. 528) indicates a small piece of the skin of the thigh with the "heat spots" horizontally and the "cold spots" vertically shaded.

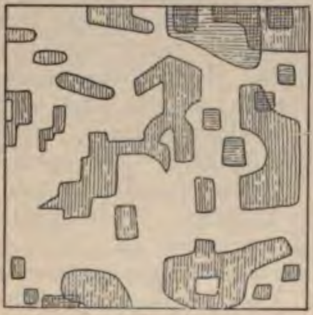
FIG. 528.—Heat and cold spots. (Waller, after Goldscheider.)

All these facts clearly indicate that different varieties of sensation are the result of the stimulation of different end organs, and that the impulses are conveyed to the central nervous system by different groups of nerve-fibres; they moreover form the clearest piece of evidence we have that pain is a distinct kind of sensation.

The question is more difficult to answer, which particular end organ is concerned with each variety of sensation. There is, however, little doubt that the nerve-fibrils around the hair follicles of the short hairs are the terminations most affected by changes of pressure, and also that Meissner's corpuscles are purely tactual, taking the place of hairs in hairless parts. In the palmar surface of the last phalanx of the index finger, there are 21 Meissner's corpuscles per square centimetre; in other parts of the palm and sole the number varies from 2 to 8. End-bulbs are believed to be the organs for cold; they are most numerous in the conjunctiva and glans penis, where "cold spots" are almost exclusively present. The end organs in "heat spots" have not been identified with certainty, but they are probably larger organs, and placed more deeply in the skin.

We have spoken of the pressure sense as the true tactile sense; but Meissner pointed out many years ago that the hand immersed in a fluid like mercury at body temperature, does not feel the contact of the fluid, although the fluid pressure may be far above the limen; it is, however, equal in all directions; it is therefore clear that the adequate stimulus for touch organs consists in a deformation of the skin surface.

As compared with the sensation obtained from pain spots, touch is quicker both in development and subsidence. Thus vibrations of strings are recognisable as such by the finger, even at a frequency of 1500 vibrations per second. A revolving wheel with toothed edge does not give a sensation of smoothness till the teeth meet the skin at the rate of from 480 to 640 per second.

Adaptation plays a part as important in cutaneous as in other sensations. The same room feels warm to a man who enters it from the street, and cold to another who has been in a conservatory. Hering calls the point of adaptation to temperature "the physiological zero." Thus the temperature of the mouth and the lips may actually differ by several degrees, yet neither of them will feel hot or cold because each is at the physiological zero temperature. Sensations of warmth or cold arise when the physiological zero is altered: they persist until a new zero is formed, *i.e.*, until adaptation is complete. So, too, heavy weights feel unduly heavy after light weights, and *vice versâ*. When eyeglasses or false teeth are first worn, their contact is well-nigh unbearable; yet later, through adaptation, the discomfort becomes negligeable.

It is very difficult to draw any hard and fast line between the cutaneous sensations hitherto described, and those which are grouped under the name "common sensibility." Sensations which are difficult to describe but which are perfectly familiar, such as those accompanying tickling, shivering, shuddering, and the like, are regarded as varieties of "common sensation." Pain may be looked upon as an excessive form of "common sensation," but cutaneous pain is so distinct a sensation that most psychologists agree to place it under a "special" rather than a "common" heading.

The term "common sensation" is most frequently employed in reference to sensations from the interior of the body, and in this connection Head's work on the relation of internal to cutaneous pain must be mentioned. To him we owe the knowledge of the spatial relationship of the associated sensations, and this is of a segmental nature. Each viscus stands in relation with a definite patch of skin; that is to say, the afferent fibres from the skin and from the viscera belong to corresponding spinal nerve-roots. Localisation of painful or uncomfortable feelings arising from disorders of internal organs is always very difficult; hence the associated skin pains play an important part in ascertaining the position of internal maladies.

Drugs.—Cocaine applied locally depresses all forms of cutaneous sensibility, but especially the true tactile sense; carbolic acid acts similarly but less strongly. Chloroform produces a temporary burning sensation, and then blunts sensibility especially to temperature changes. Menthol produces a feeling of local cold because it first causes hyperæsthesia of the end organs for cold; this is followed by a depression of the same end organs.

The Muscular or Kinæsthetic Sense.

By the muscular sense we become aware that movement is taking place in some part of the body. We are especially conscious of willed muscular action, and the muscular sense has thus been confused and identified with the "feeling of innervation," or "sense of effort," which accompanies volitional movements. By some this feeling has been attributed to a direct discharge from the motor to the sensory cells of the cerebral cortex occurring at the very birth of the efferent impulse. But most physiologists of the present day regard the sense of effort as due to afferent impulses peripherally generated by the accompanying respiratory and other strains; and they no longer consider it as a very important factor in effecting or estimating movement. It is in the estimation of weights that the value of peripheral sensations to the muscular sense can be most clearly seen.

When a weight is first handled, the amount of force necessary to lift it is estimated in the light of past experience. As it is being lifted, sensations from the moving limb guide the expenditure of force: a weight which flies up too fast or does not move, at once calls for less or more muscular force. Similarly the muscular sense is invoked when we estimate the extent to which we have moved our limbs, or to which they have been passively moved by others.

These guiding sensations are not merely of cutaneous origin. Persons whose skin has been rendered insensitive by cocaine, or by certain diseases, yet retain the power of estimating weights and the extent of their movement. In locomotor ataxy the muscular sense may be destroyed while the skin retains its usual sensitiveness to touch. On the other hand, we must remember that it is not at all certain that the muscles are solely or even predominately the seat of these peripheral sensations, and that therefore "kinæsthetic sense" is a term preferable to "muscular sense." It is true that sensory end-organs and nerve-fibres occur in muscles and tendons, which presumably transmit impulses upon change of muscular form or of tendinous strain. But we have experimental evidence that the pressure and movement of joint-surfaces are important factors in the development of kinæsthetic sensations. The "muscular sense" is thus of very complex origin.

CHAPTER LIII

TASTE AND SMELL

Taste.

CERTAIN anatomical facts must be studied first in connection with the tongue, the upper surface of which is concerned in the reception of taste stimuli.

The tongue is a muscular organ covered by mucous membrane. The muscles, which form the greater part of the substance of the tongue (*intrinsic* muscles) are termed *linguales;* and by these, which are attached to the mucous membrane, its smaller and more delicate movements are performed.

By other muscles (*extrinsic* muscles), like the genio-hyoglossus, the styloglossus, etc., the tongue is fixed to the surrounding parts; and by these its larger movements are performed.

Its mucous membrane resembles other mucous membranes in essential points, but contains *papillæ*, peculiar to itself. The tongue is also beset with mucous glands (fig. 530) and lymphoid nodules.

The lingual *papillæ* are thickly set over the anterior two-thirds of its upper surface, or *dorsum* (fig. 529), and give to it its characteristic roughness. Three principal varieties may be distinguished, namely, the (1) *circumvallate*, the (2) *fungiform*, and the (3) *conical and filiform* papillæ. They are all formed by a projection of the corium of the mucous membrane, covered by stratified epithelium; they contain special branches of blood-vessels and nerves. The corium in each kind is studded by microscopic papillæ.

(1.) *Circumvallate.*—These papillæ (fig. 531), eight or ten in number, are situate in a V-shaped line at the base of the tongue (1, 1, fig. 529). They are circular elevations, from $\frac{1}{20}$th to $\frac{1}{12}$th of an inch wide (1 to 2 mm.), each with a slight central depression, and surrounded by a circular moat, at the outside of which again is a slightly elevated ring or rampart; their walls contain taste-buds. Into the moat that surrounds the central tower, a few little glands (*glands of Ebner*) open. They form a thin, watery secretion.

(2.) *Fungiform.*—The fungiform papillæ (3, fig. 529) are scattered chiefly over the sides and tip, and sparingly over the middle of the dorsum, of the tongue; their name is derived from their being shaped like a puff-ball fungus. (See fig. 532, B.)

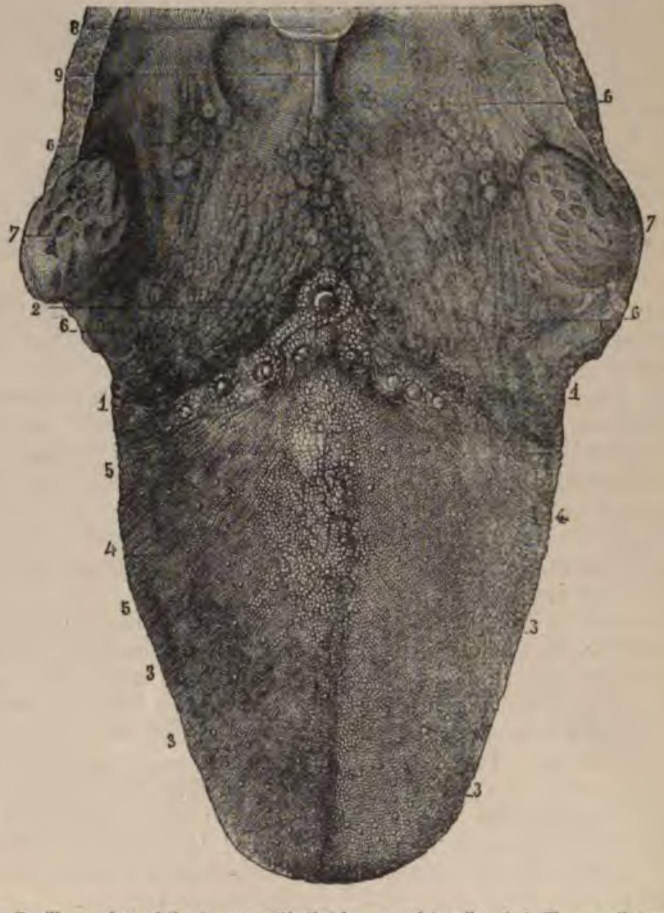

FIG. 529.—Papillar surface of the tongue, with the fauces and tonsils. 1, 1, Circumvallate papillæ in front of 2, the foramen cæcum; 3, fungiform papillæ; 4, filiform and conical papillæ; 5, transverse and oblique rugæ; 6, mucous glands at the base of the tongue and in the fauces; 7, tonsils; 8, part of the epiglottis; 9, median glosso-epiglottidean fold (frænum epiglottidis). (From Sappey.)

(3.) *Conical and Filiform.*—These, which are the most abundant papillæ, are scattered over the whole upper surface of the tongue, but especially over the middle of the dorsum. They vary in shape, some being conical (simple or compound) and others filiform; they are covered by a thick layer of epithelium, which is either arranged over them, in an imbricated manner, or is prolonged from their surface in the form of fine stiff projections (fig. 533). In carnivora they are developed into horny spines. From their structure, it is likely that these papillæ have a mechanical and tactile function, rather than that of taste; the latter sense is seated especially in the other two varieties of papillæ, the *circumvallate* and the *fungiform*.

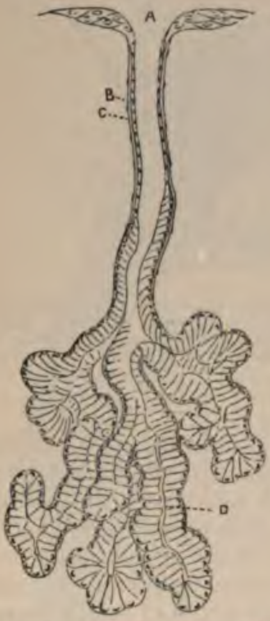

FIG. 530.—Section of a mucous gland from the tongue. A, Opening of the duct on the free surface; C, basement membrane with nuclei; B, flattened epithelial cells lining duct. The duct divides into several branches, which are convoluted and end blindly, being lined throughout by columnar epithelium. D, lumen of one of the tubuli of the gland. × 90. (Klein and Noble Smith.)

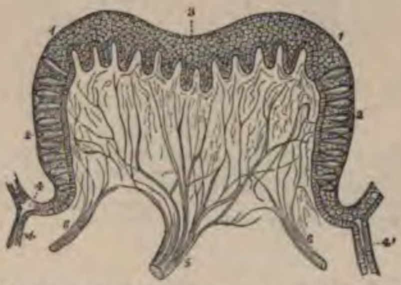

FIG. 531.—Vertical section of a circumvallate papilla of the calf. 1 and 3, Epithelial layers covering it; 2, taste-buds; 4 and 4′, duct of serous gland opening out into the pit in which papilla is situated; 5 and 6, nerves ramifying within the papilla. (Engelmann.)

In the circumvallate papillæ of the tongue of man peculiar structures known as *taste-buds* are found. They are of an oval shape, and consist of a number of closely packed, very narrow and fusiform, cells (*gustatory cells*). This central core of gustatory cells is enclosed in a single layer of broader fusiform cells (*encasing cells*). The gustatory cells terminate in fine stiff pikes which project on the free surface (fig. 534, *a*).

These bodies also occur in considerable numbers in the epithelium of the papilla foliata, which is situated near the root of the tongue in the rabbit, and is composed of a number of closely packed papillæ very similar to the circumvallate papillæ of man. Taste-buds are also scattered over the posterior third of the tongue and the pharynx, as low as the posterior (laryngeal) surface of the epiglottis.

The gustatory cells in the interior of the taste-buds are surrounded by arborisations of nerve-fibres.

The middle of the dorsum of the tongue is not endowed to any great degree with the sense of taste; the tip and margins, and especially the posterior third of the dorsum (*i.e.*, in the region of the taste-buds), possess this faculty. The anterior part of the tongue is supplied by the lingual branch of the fifth nerve and the chorda tympani, and the posterior third by the glosso-pharyngeal nerve. Considerable discussion has arisen whether there is more than one nerve of taste. The view generally held is that the glosso-pharyngeal nerve is the nerve of taste, and the lingual the nerve of tactile sensation. Nevertheless, the lingual and the chorda tympani do contain taste-fibres, which probably take origin from the cells of the geniculate ganglion; the central axons of these cells pass by the pars intermedia to the sensory nucleus of the glosso-pharyngeal nerve. Gowers holds that the fifth nerve is the only nerve of taste, and has recorded a case of loss of taste where the fifth nerve alone was the seat of disease; other cases, however, do not support this view.

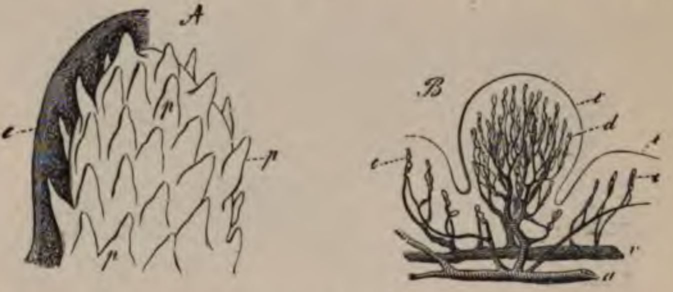

FIG. 532.—Surface and section of the fungiform papillæ. A, The surface of a fungiform papilla, partially denuded of its epithelium; *p*, secondary papillæ; *e*, epithelium. B, section of a fungiform papilla with the blood-vessels injected; *a*, artery; *v*, vein; *c*, capillary loops of similar papillæ in the neighbouring structure of the tongue; *d*, capillary loops of the secondary papillæ; *e*, epithelium. (From Kölliker, after Todd and Bowman.)

Tastes may be classified into—

1. Sweet. 2. Bitter.
3. Acid. 4. Saline.

Whether alkaline and metallic tastes are elementary, is as yet undecided. All the above affect to a varying extent the nerves of tactile sense as well of those of touch proper, sweet having the least, acids the most marked action upon the latter. Sweet tastes are best appreciated by the tip, acid by the side, and bitter tastes by the back of the tongue.

The substance to be tasted must be dissolved; here there is a striking contrast to the sense of smell; flavours are really odours. In testing the sense of taste in a patient, the tongue should be protruded, and drops of the substance to be tasted applied with a camel's hair brush to the different parts; the subject of the experiment must signify his sensations by signs, for if he withdraws the tongue to speak, the material gets widely spread. The more concentrated the solution, and the larger the surface acted on, the more intense is the taste; some tastes are perceived more rapidly than others, saline tastes the most rapidly of all. The best temperature of the substance to be tasted is from 10° to 35° C. Very high or very low temperatures deaden the sense.

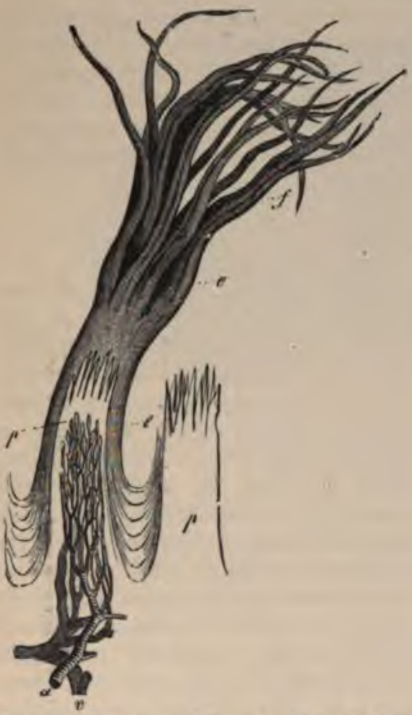

FIG. 533.—Filiform papillæ, one with epithelium, the other without. $\frac{35}{1}$.—*p*, The substance of the papillæ dividing at their upper extremities into secondary papillæ; *a*, artery, and *v*, vein, dividing into capillary loops; *e*, epithelial covering, laminated between the papillæ, but extended into hair-like processes, *f*, from the extremities of the secondary papillæ. (From Kölliker, after Todd and Bowman.)

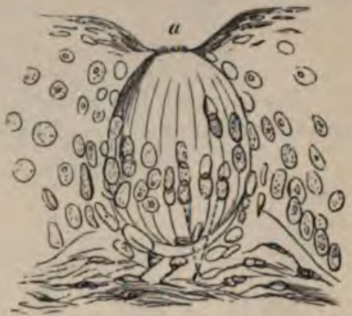

FIG. 534.—Taste-bud from dog's epiglottis (laryngeal surface near the base), precisely similar in structure to those found in the tongue. *a*, Depression in epithelium over bud; below the letter are seen the fine hair-like processes in which the cells terminate; *c*, two nuclei of the axial (gustatory) cells. The more superficial nuclei belong to the superficial (encasing) cells; the converging lines indicate the fusiform shape of the encasing cells. × 400. (Schofield.)

Individual papillæ, when thus treated with various solutions, show great diversity: from some only one or two tastes can be evoked, from others all four. The papillæ may also be stimulated electrically.

It is possible by chewing the leaves of an Indian plant (Gymnema sylvestre) to do away with the power of tasting bitters and sweets, while the taste for acids and salts remains.

It will thus be seen that there are many facts pointing to the conclusion, that the varieties of gustatory like those of cutaneous sensation are due to the stimulation of different end organs.

When diluted sweet and salt solutions are simultaneously applied to the tongue, they tend to neutralise one another, but a true indifferent point is difficult or impossible to reach. Sweet and bitter, sweet and acid-tasting substances are antagonistic to a similar but less perfect extent. Contrast-effects of one taste upon another are matters of common observation, but can only be experimentally investigated with great difficulty.

Smell.

The entrance to the nasal cavity is lined with a mucous membrane closely resembling the skin. The greater part of the rest of the cavity is lined with ciliated epithelium; the corium is thick and contains numerous mucous glands. The olfactory region in man is limited to a portion of the membrane covering the upper turbinal bone, and is only 245 square millimetres in area. This area is larger in animals with a keener sense of smell than we possess. The cells of the epithelium here are of several kinds:—first, columnar cells not ciliated (fig. 535, *st*), with the broad end at the surface, and below tapering into an irregular branched process or processes, the terminations of which pass into the next layer: the second kind of cell (fig. 535, *r*) consists of a small cell body with large spherical nucleus, situated between the ends of the first kind of cell, and sending upwards a process to the surface between the cells of the first kind, and from the other pole of the nucleus a process towards the corium. The latter process is very delicate and may be varicose. The upper process is prolonged beyond the surface, where it becomes stiff, and in some animals, like the frog, is provided with hairs. These cells, which are called *olfactorial cells*, are numerous, and the nuclei of the cells not being on the same level, a comparatively thick nuclear layer is the result (fig. 537, *b*). In the corium are a number of serous glands called Bowman's glands. They open upon the surface by fine ducts passing up between the epithelium cells.

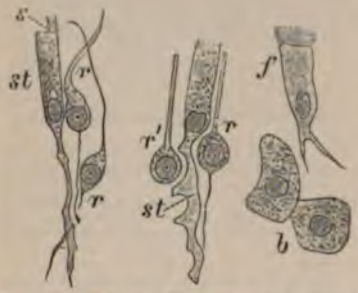

FIG. 535.—Cells from the olfactory region of the rabbit. *st*, Supporting cells; *r*, *r'*, olfactorial cells; *f*, ciliated cells; *s*, cilia-like processes; *b*, cells from Bowman's gland. (Stöhr.)

The distribution of the olfactory nerves which penetrate the cribriform plate of the ethmoid bone and pass to this region of the nasal mucous membrane is shown in fig. 536. The nerve-fibres are continuous with the inner processes of the cells we have termed olfactorial; the columnar cells between these act as supports to them.

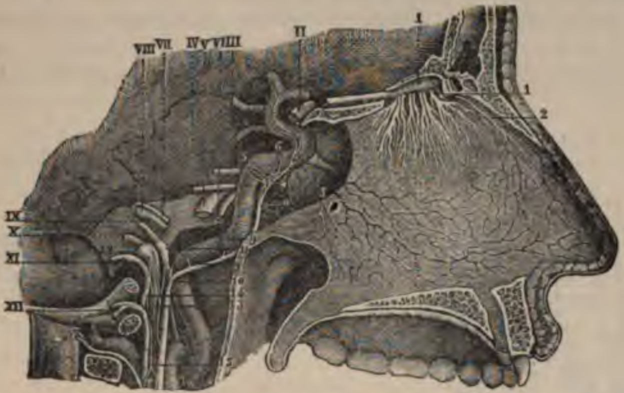

FIG. 536.—Nerves of the septum nasi, seen from the right side. ⅔.—I, The olfactory bulb; 1, the olfactory nerves passing through the foramina of the cribriform plate, and descending to be distributed on the septum; 2, the internal or septal twig of the nasal branch of the ophthalmic nerve; 3, naso-palatine nerves. (From Sappey, after Hirschfeld and Leveillé.)

The olfactory tract is an outgrowth of the brain which was originally hollow, and remains so in many animals; in man the cavity is obliterated, and the centre is occupied by neuroglia: outside this the white fibres lie, and a thin superficial layer of neuroglia covers these. The three "roots" of the olfactory tract have been traced to the uncinate gyrus and hippocampal regions of the same side of the brain, which is the portion experimentally found to be associated with the reception of olfactory impulses (see p. 690). From the cells of the grey matter here fibres pass by a complex path to the corresponding regions of the opposite side. There is also a communication *viâ* the corpora mammillaria with the optic thalamus and tegmentum of the mid-brain.

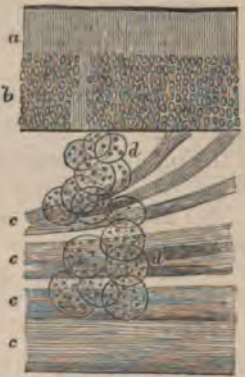

FIG. 537. — Semi-diagrammatic section through the olfactory mucous membrane of the new-born child. *a*, Non-nuclear; and *b*, nucleated portions of the epithelium; c, nerves; *dd*, Bowman's glands. (M. Schultze.)

The olfactory bulb has a more complicated structure; above there is first a continuation of the olfactory tract (white fibres enclosing neuroglia); below this four layers are distinguishable; they are shown in the accompanying diagram from Ramon y Cajal's work, the histological method used being Golgi's.

(1) A layer of white fibres containing numerous small cells, or "*granules*" (D).

(2) A layer of large nerve-cells called "*mitral cells*" (C), with smaller cells (*a*) mixed with them. The axis-cylinder processes of these cells pass up into the layer above and eventually become fibres of the olfactory tract E, which passes to the grey matter of the base of the brain F. They give off numerous collaterals on the way (*e*,*f*).

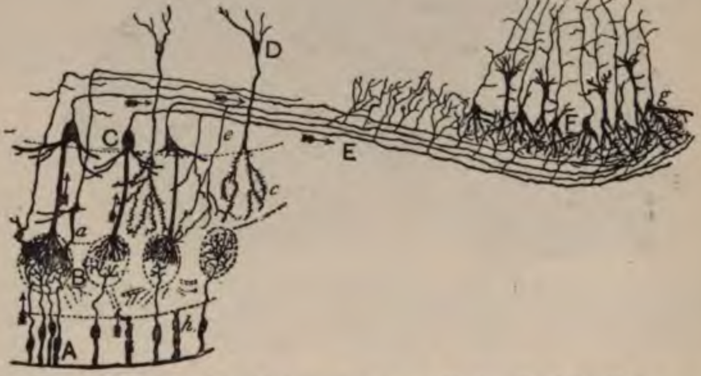

FIG. 538.—Nervous mechanism of the olfactory apparatus. A, Bipolar cells of the olfactory apparatus (Max Schultze's olfactorial cells); B, olfactory glomeruli; C, mitral cells; D, granule of white layer; E, external root of the olfactory tract; F, grey matter of the sphenoidal region of the cortex; *a*, small cell of the mitral layer; *b*, basket of a glomerulus; *c*, spiny basket of a granule; *e*, collateral of the axis-cylinder process of a mitral cell; *f*, collaterals terminating in the molecular layer of the frontal and sphenoidal convolutions; *g*, superficial triangular cells of the cortex; *h*, supporting epithelium cells of the olfactory mucous membrane. (Ramon y Cajal.)

(3) The layer of *olfactory glomeruli* (B). Each glomerulus is a basket-work of fibrils derived on the one hand from the terminal arborisations of the mitral cells, and on the other from similar arborisations of the non-medullated fibres which form the next layer.

(4) *The layer of olfactory nerve-fibres.*—These are non-medullated; they continue upwards the *bipolar olfactory cells*, or as we have already termed them, the olfactorial cells of the mucous membrane.

Animals may be divided into three classes:—those which, like the porpoise, have no sense of smell (*anosmatic*); those which possess it in comparatively feeble degree (man, most primates, monotremes, and some cetacea); those are called *microsmatic*. In man the thickness of the olfactory membrane is only 0·06 mm. Most mammals are in contra-distinction *macrosmatic*, the thickness of the membrane being 0·1 mm. or more, and its area larger.

The mucous membrane must be neither too dry nor too moist; if we have a cold we are unable to smell odours or flavours (which are really odours). When liquids are poured into the nose, their smell is imperceptible, as they damage the olfactory epithelium, owing to the difference of osmotic pressure. But even if a "normal" saline solution of an odorous substance be substituted, the sense of smell is still lost so long as air-bubbles are carefully excluded from the nasal cavity. It is therefore necessary that odorous substances should be in a gaseous state in order to act upon the olfactory epithelium; they are propagated mainly by diffusion.

Generally, the odours of homologous series of compounds increase in intensity with increase of molecular weight, but bodies of very low molecular weight are odourless, while vapours of very high molecular weight, which escape and diffuse slowly have little or no smell. A slight change in chemical constitution may produce marked alteration in the character of the odour of a substance; certain modes of atomic grouping within the molecule appear to be more odoriferous than others. Attempts have been made to discover the elementary sensations of smell, but hitherto with scant success. Many odours have unquestionably a complex physiological effect. For example, when nitrobenzol is held before the nose, it yields first the smell of heliotrope, next the smell of bitter almonds, and finally the smell of benzene; just as if different end-organs became successively exhausted. Some substances have a very different smell according to their concentration. Chemical dissociation, too, unquestionably plays a prominent part.

Nevertheless, there are certain points which indicate the existence of primary sensations of smell. First, some persons are congenitally insensible to one or more odours, but yet smell others quite normally. Hydrocyanic acid, mignonette, violet, vanilla, benzoin, are substances which appear to certain people to have no smell. Secondly, some odorous bodies, when simultaneously given, antagonise one another; others produce a mixed smell. Thirdly, fatigue of the epithelium with one odour will modify or abolish the effect of some smells, but will leave that of others untouched.

The delicacy of the sense of smell is most remarkable. Valentin calculates that even $\frac{3}{100,000,000}$ of a grain of musk can be distinctly smelled. Solutions of camphor afford a good means of testing olfactory acuity. One tube of camphor solution is presented to the subject along with three tubes of water, and the former is replaced with weaker and weaker solutions until it is indistinguishable from the tubes containing water. Pungent substances, like ammonia, are unsuited for olfactometrical experiment. They stimulate the endings of the fifth as well as those of the olfactory nerve.

CHAPTER LIV

HEARING

Anatomy of the Ear.

THE Organ of Hearing (fig. 539) is divided into three parts, (1) the external, (2) the middle, and (3) the internal ear. The two first are only accessory to the third or internal ear, which contains the essential parts of the organ of hearing.

External Ear.—The external ear consists of the *pinna* and the *external auditory meatus.*

The principal parts of the *pinna* are two prominent rims enclosed one within the other (*helix* and *antihelix*), and enclosing a central hollow named the *concha;* in front of the concha is a prominence directed backwards, the *tragus,* and opposite to this one directed forwards, the *antitragus.* From the concha, the auditory canal, with a slight arch directed upwards, passes inwards and a little forwards to the membrana tympani, to which it thus serves to convey the vibrating air. Its outer part consists of fibro-cartilage continued from the concha, its inner part of bone. Both are lined by skin continuous with that of the pinna; the skin also extends over the outer surface of the *membrana tympani.* Towards the outer part of the canal are fine hairs and sebaceous glands, while deeper in the canal are small glands, resembling the sweat-glands in structure, which secrete the *cerumen* or wax of the ear.

Middle Ear or **Tympanum.**—The middle ear, or tympanum or drum (3, fig. 539), is separated by the *membrana tympani* from the external auditory meatus. It is a cavity in the temporal bone, opening through its anterior and inner wall into the Eustachian tube, a cylindriform flattened canal, dilated at both ends, composed partly of bone and partly of elastic cartilage, and lined with mucous membrane, which forms a communication between the tympanum and the pharynx. It opens into the cavity of the pharynx just behind the posterior aperture of the nostrils. The cavity of the tympanum communicates posteriorly with air-cavities, the *mastoid cells* in the mastoid process of the temporal bone; but its only opening to the external air is through the Eustachian tube (4, fig. 539). The walls of the tympanum are osseous, except where apertures in them are closed with membrane, as at the *fenestra rotunda*, and *fenestra ovalis*, and at the outer part where the bone is replaced by the membrana tympani. The cavity of the tympanum is lined with mucous membrane, the epithelium of which is ciliated and continuous through the Eustachian tube with that of the pharynx. In some parts, however, viz., over the roof, promontory, ossicles, and membrana tympani, the epithelium is of the pavement variety and is destitute of cilia. A chain of small bones extends from the membrana tympani to the fenestra ovalis.

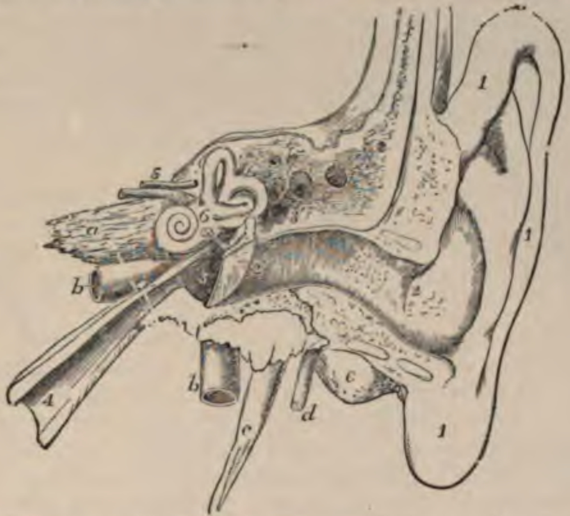

FIG. 539.—Diagrammatic view from before of the parts composing the organ of hearing of the left side. The temporal bone of the left side, with the accompanying soft parts, has been detached from the head, and a section has been carried through it transversely, so as to remove the front of the meatus externus, half the tympanic membrane, the upper and anterior wall of the tympanum and Eustachian tube. The meatus internus has also been opened, and the bony labyrinth exposed by the removal of the surrounding parts of the petrous bone. 1, The pinna and lobe; 2, meatus externus; 2', membrana tympani; 3, cavity of the tympanum; 3', its opening backwards into the mastoid cells; between 3 and 3', the chain of small bones; 4, Eustachian tube; 5, meatus internus, containing the facial (uppermost) and the auditory nerves; 6, placed on the vestibule of the labyrinth above the fenestra ovalis; *a*, apex of the petrous bone; *b*, internal carotid artery: *c*, styloid process; *d*, facial nerve issuing from the stylo-mastoid foramen; *e*, mastoid process; *f*, squamous part of the bone covered by integument, etc. (Arnold.)

The *membrana tympani* is placed in a slanting direction at the bottom of the external auditory canal, its plane being at an angle of about 45° with the lower wall of the canal. It is formed of fibres, some running radially, some circularly; its margin is set in a bony groove; its outer surface is covered with a continuation of the cutaneous lining of the auditory canal, its inner surface with the mucous membrane of the tympanum.

The *ossicles* are three in number; named malleus, incus, and stapes. The malleus, or hammer-bone, has a long slightly-curved process, called its handle, which is inserted between the layers of the membrana tympani; the line of attachment is vertical, including the whole length of the handle, and extending from the upper border to the centre of the membrane. The head of the malleus is irregularly rounded; its neck, or the line of boundary between the head and the handle, supports two processes: a *short* conical one, and a *slender* one, *processus gracilis,* which extends forwards, and is attached to the wall of the cavity at the Glaserian fissure. The *incus,* or anvil-bone, shaped like a bicuspid molar tooth, is articulated by its broader part, corresponding with the surface of the crown of the tooth, to the malleus. Of its two fang-like processes, one, directed backwards, has a free end attached by ligament to a depression in the mastoid bone; the other, curved downwards, longer and more pointed, articulates by means of a roundish tubercle, formerly called *os orbiculare,* with the *stapes,* a little bone shaped like a stirrup, of which the base fits into the membrane of the fenestra ovalis. To the neck of the stapes, a short process, corresponding with the loop of the stirrup, is attached the *stapedius* muscle.

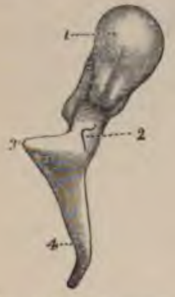

FIG. 540.—The hammer-bone or malleus, seen from the front. 1, The head; 2, neck; 3, short process; 4, handle. (Schwalbe.)

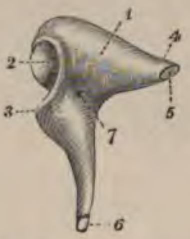

FIG. 541.—The incus, or anvil-bone. 1, Body; 2, ridged articulation for the malleus; 4, processus brevis, with 5, rough articular surface for ligament of incus; 6, processus magnus, with articulating surface for stapes; 7, nutrient foramen. (Schwalbe.)

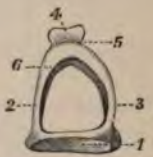

FIG. 542.—The stapes, or stirrup-bone. 1, Base; 2 and 3, arch; 4, head of bone, which articulates with orbicular process of the incus; 5, constricted part of neck; 6, one of the crura. (Schwalbe.)

The muscles of the tympanum are two in number. The *tensor tympani* arises from the cartilaginous end of the Eustachian tube and the adjoining surface of the sphenoid, and from the sides of the canal in which the muscle lies; the tendon of the muscle bends at nearly a right angle over the end of the processus cochleariformis, and is inserted into the inner part of the handle of the malleus. The *stapedius* is concealed within a canal in the bone in front of the aqueductus Fallopii. The tendon issues from the aperture of this canal and is inserted into the neck of the stapes posteriorly.

The Internal Ear.—The proper organ of hearing is formed by the distribution of the auditory nerve, within the internal ear, or *labyrinth,* a set of cavities within the petrous portion of the temporal bone. The bone which forms the walls of these cavities is denser than that around it, and forms the *osseous labyrinth;* the membrane within the cavities forms the *membranous labyrinth.* The membranous labyrinth contains a fluid called *endolymph;* while outside it, between it and the osseous labyrinth, is a fluid called *perilymph.* This fluid is not pure lymph, as it contains mucin.

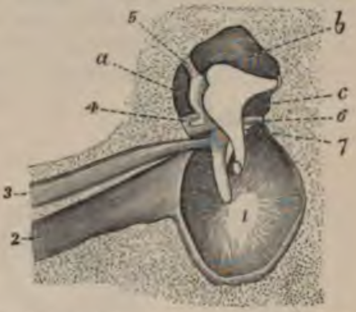

FIG. 543.—Interior view of the tympanum, with membrana tympani and bones in natural position. 1, Membrana tympani; 2, Eustachian tube; 3, tensor tympani muscle; 4, lig. mallei exter.; 5, lig. mallei super.; 6, chorda-tympani nerve; *a*, *b*, and *c*, sinuses about ossicles. (Schwalbe.)

The **Osseous Labyrinth** consists of three principal parts, namely, the *vestibule*, the *cochlea*, and the *semicircular canals.*

The *vestibule* is the middle cavity of the labyrinth, and the central chamber of the auditory apparatus. It presents, in its inner wall, several openings for the entrance of the divisions of the auditory nerve; in its outer wall, the *fenestra ovalis* (2, fig. 544*a*), an opening filled by membrane, in which is inserted the base of the stapes; in its posterior and superior walls, five openings by which the *semicircular canals* communicate with it: in its anterior wall, an opening leading into the *cochlea.* The structure of the *semicircular canals* is described in Chapter XLIX.

The *cochlea* (6, 7, 8, fig. 544*a*, and 8, fig. 544*b*) is shaped like a snail-shell, and is situated in front of the vestibule; its base rests on the bottom of the internal meatus, where some apertures transmit to it the cochlear filaments of the auditory nerve. In its axis, the cochlea is traversed by a conical column, the *modiolus*, around which a *spiral canal* winds with two turns and a half from the base to the apex. At the apex of the cochlea the canal is closed; at the base it presents three openings, of which one, already mentioned, communicates with the vestibule; another, called *fenestra rotunda*, is separated by a membrane from the cavity of the tympanum; the third is the orifice of the *aquæductus cochleæ*, a canal leading to the jugular fossa of the petrous bone. The spiral canal is divided into two passages, or *scalæ* (staircases), by a partition formed partly of bone, the *lamina spiralis*, connected with the modiolus, and partly of a membrane called the *basilar membrane.*

The **Membranous Labyrinth.**—The membranous labyrinth corresponds generally with the form of the osseous labyrinth, so far as regards the vestibule and semicircular canals, but is separated from the walls of these parts by perilymph, except where the nerves enter into connection within it. The labyrinth is a closed membrane containing endolymph, which is of much the same composition as perilymph, but contains less solid matter. It is somewhat viscid, as is the perilymph, and it is secreted by the epithelium lining its cavity; all the sonorous vibrations impressing the auditory nerves in these parts of the internal ear, are conducted through fluid to a membrane suspended in and containing fluid. In the cochlea, the membranous labyrinth completes the septum between the two *scalæ*, and encloses a spiral canal, called the *canalis cochleæ* (fig. 545). The fluid in the *scalæ* of the cochlea is continuous with the perilymph in the vestibule and semicircular canals. The vestibular portion of the membranous labyrinth comprises two communicating cavities, of which the larger and upper is named the *utricle;* the lower, the *saccule.* They are lodged in depressions in the bony labyrinth, termed respectively *fovea hemielliptica* and *fovea hemispherica.* The membranous semicircular canals open into the utricle; the canal of the cochlea opens by the canalis reuniens into the

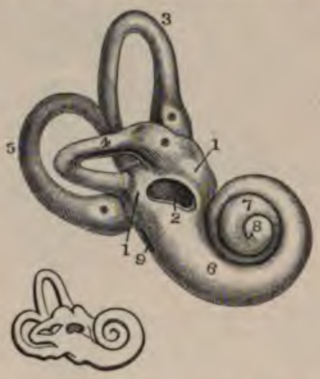

FIG. 544*a*.—Right bony labyrinth, viewed from the outer side. The specimen here represented is prepared by separating piecemeal the looser substance of the petrous bone from the dense walls which immediately enclose the labyrinth. 1, The vestibule; 2, fenestra ovalis; 3, superior semicircular canal; 4, horizontal or external canal; 5, posterior canal; *, ampullæ of the semicircular canals; 5, first turn of the cochlea; 7, second turn; 8, apex; 9, fenestra rotunda. The smaller figure in outline below shows the natural size. $\frac{2\frac{1}{2}}{1}$. (Sömmering.)

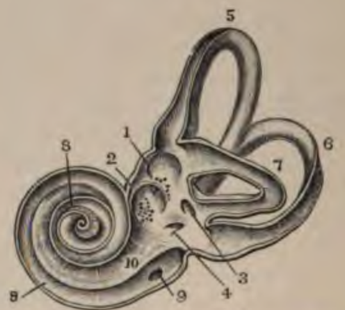

FIG. 544*b*.—View of the interior of the left labyrinth. The bony wall of the labyrinth is removed superiorly and externally. 1, Fovea hemielliptica; 2, fovea hemispherica; 3, common opening of the superior and posterior semicircular canals; 4, opening of the aqueduct of the vestibule; 5, the superior; 6, the posterior, and 7, the external semicircular canals; 8, spiral tube of the cochlea (scala tympani); 9, opening of the aqueduct of the cochlea; 10, placed on the lamina spiralis in the scala vestibuli. $\frac{2\frac{1}{2}}{1}$. (Sömmering.)

saccule. The accompanying diagram (fig. 545) shows the relationship of all these parts to one another.

Auditory Nerve.—All the organs now described are provided for the appropriate exposure of the filaments of the auditory nerve to vibrations. It enters the bony canal (the *meatus auditorius internus*), with the facial nerve and the nervus intermedius, and, traversing the bone, enters the labyrinth at the angle between the base of the cochlea and the vestibule, in two divisions; one for the vestibule and semicircular canals, and the other for the cochlea.

There are two branches for the vestibule, one, superior, distributed to the utricle and to the superior and horizontal semicircular canals, and the other, inferior, which arises from the cochlear nerve, ends in the saccule and posterior semicircular canal. There can, however, be little doubt that the inferior nerve, although it is contained for some distance in the sheath of the cochlear nerve, is really composed of vestibular fibres. The terminations of the nerve in the saccule, utricle, and semicircular canals have been already described in page 707; so we can pass at once to the cochlea.

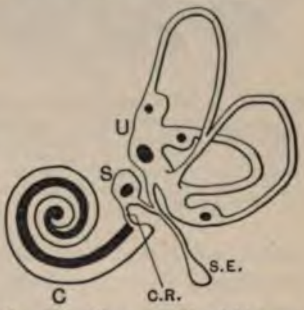

FIG. 545.—Diagram of the right membranous labyrinth. U, Utricle, into which the three semicircular canals open; S, saccule, communicating with the cochlea (C) by C.R., the canalis reuniens, and with the utricle by a canal having on it an enlargement, the saccus endolymphaticus (S.E.). The black shading represents the places of termination of the auditory nerve, namely, in the maculæ of the utricle and saccule; the cristæ in the ampullary ends of the three semicircular canals; and in the whole length of the canal of the cochlea. (After Schäfer.)

This is best seen in vertical section; the cavity is divided partly by bone (the *spiral lamina*), partly by membrane (the *basilar membrane*), into two spiral scalæ, the *scala tympani* and *scala vestibuli* (fig. 546). The basilar membrane increases in breadth from the base towards the apex of the cochlea. It contains fibres (about 24,000 in all) embedded in a homogeneous matrix, and running radially straight from the spiral lamina to the *spiral ligament*, where its other end is again attached to the bone. At the apex of the cochlea, the lamina ends in a small *hamulus*, the inner and concave part of which being detached from the summit of the modiolus, leaves a small aperture named the *helicotrema*, by which the two scalæ, separated in all the rest of their length, communicate.

Besides the scala vestibuli and scala tympani, there is a third space between them, called *scala media* or *canal of the cochlea* (CC, fig. 547). In section it is triangular, its external wall being formed by the wall of the cochlea, its upper wall (separating it from the scala vestibuli) by the membrane of Reissner, and its lower wall (separating it from the scala tympani) by the basilar membrane, these two meeting at the outer edge of the bony lamina spiralis. Following the turns of the cochlea to its apex, the scala media there terminates blindly; while towards the base of the cochlea it is also closed, with the exception of a very narrow passage (canalis reuniens) uniting it with the saccule. The scala media (like the rest of the membranous labyrinth) contains *endolymph.*

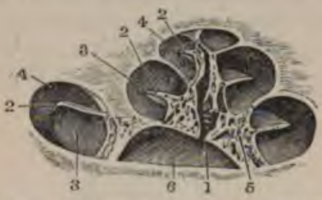

FIG. 546.—View of the osseous cochlea divided through the middle. 1, Central canal of the modiolus; 2, lamina spiralis ossea; 3, scala tympani; 4, scala vestibuli; 5, porous substance of the modiolus near one of the sections of the canalis spiralis modioli. $\frac{5}{1}$ (Arnold.)

Organ of Corti.—Upon the basilar membrane are arranged cells of various shapes. About midway between the outer edge of the lamina spiralis and the outer wall of the cochlea are situated the *rods of Corti.* Viewed sideways, they are seen to consist of an external and internal pillar, each rising from an expanded foot or *base* attached to the basilar membrane (*o*, *n*, fig. 548). They slant inwards towards each other, and each ends in a swelling termed the *head;* the head of the inner pillar overlies that of the outer (fig. 548). Each pair of pillars forms a pointed roof arching over a space, and by a succession of them a tunnel is formed.

There are about 3000 of these pairs of pillars, in proceeding from the base of the cochlea towards its apex. They are found progressively to increase in length, and become more oblique; in other words the tunnel becomes wider, but diminishes in height as we approach the apex of the cochlea. Leaning against the rods of Corti are certain other cells called *hair-cells,* which terminate in small hair-like processes. There are several rows of these on the outer and one row on the inner side. Between them are certain supporting cells called *cells of Deiters* (fig. 548, *x*). This structure rests upon the basilar membrane; it is roofed in by a fenestrated membrane or lamina reticularis into the fenestræ of which the tops of the various rods and cells are received. When viewed from

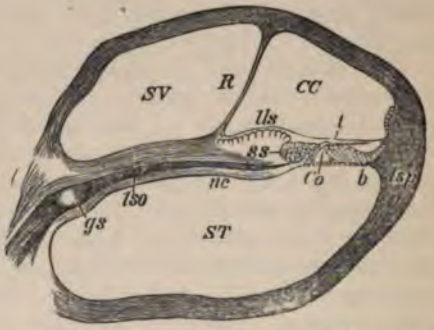

FIG. 547.—Section through one of the coils of the cochlea (diagrammatic). *ST*, Scala tympani; *SV*, scala vestibuli; *CC*, canalis cochlea or canalis membranaceus; *R*, membrane of Reissner; *lso*, lamina spiralis ossea; *lls*, limbus laminæ spiralis; *ss*, sulcus spiralis; *nc*, cochlear nerve; *gs*, ganglion spirale; *t*, membrana tectoria (below the membrana tectoria is the lamina reticularis); *b*, membrana basilaris; *Co*, rods of Corti; *lsp*, ligamentum spirale. (Quain.)

above, the organ of Corti shows a remarkable resemblance to the keyboard of a piano. The top of the organ is roofed by the *membrana tectoria* (fig. 547, *t*) that extends from the end of the limbus (*lls*, fig. 547), a connective tissue structure on the spiral lamina. The *spiral ganglion* from which the cochlear nerve-fibres originate is situated in the spiral lamina. The peripheral axons of its bipolar cells arborise around the hair-cells of the organ of Corti: the central axons pass down the modiolus, and thence to the pons (see p. 642).

Physiology of Hearing.

Sounds are caused by vibrations; when a piano-string is struck, it is thrown into a series of rapid regular vibrations; the more rapidly the vibrations occur the higher is the *pitch* of the musical note; the greater the amplitude of the vibration, the louder or more intense is the tone; if the vibrations are regular and simple (pendular), the tone is pure; if they are regular but compound, the tone is impure, and its quality or *timbre* is dependent on the rate and amplitude of the simple vibrations of which the compound vibrations are composed. The vibrations are transmitted as waves, and ultimately affect the hair-cells at the extremities of the auditory nerve in the cochlea. The semicircular canals are not concerned in the sense of hearing; their function in connection with equilibration is described in Chapter XLIX. The external and

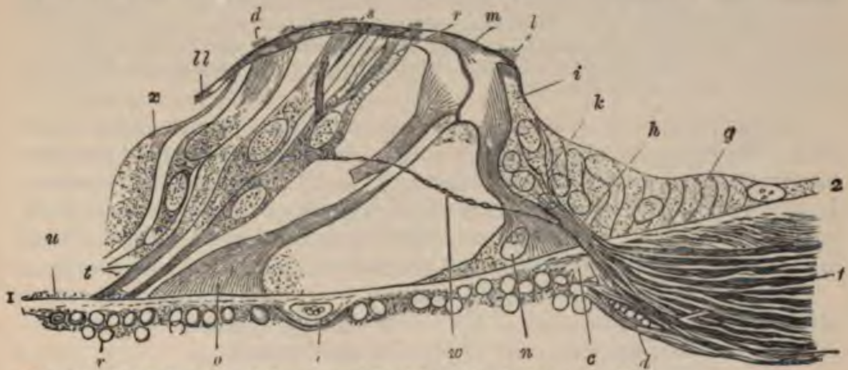

FIG. 548.—Vertical section of the organ of Corti from the dog. 1 to 2, Homogeneous layer of the membrana basilaris; *u*, vestibular layer; *v*, tympanal layer, with nuclei and protoplasm; *a*, prolongation of tympanal periosteum of lamina spiralis ossea; *c*, thickened commencement of the membrana basilaris near the point of perforation of the nerves *h*; *d*, blood-vessel (vas spirale); *e*, blood-vessel; *f*, nerves; *g*, the epithelium of the sulcus spiralis internus; *i*, internal hair-cell, with basal process *k*, surrounded with nuclei and protoplasm (of the granular layer), into which the nerve-fibres radiate; *l*, hairs of the internal hair-cell; *n*, base or foot of inner pillar of organ of Corti; *m*, head of the same uniting with the corresponding part of an external pillar, whose under half is missing, while the next pillar beyond, *o*, presents both middle portion and base; *r*, *s*, *d*, three external hair-cells; *t*, bases of two neighbouring hair or tufted cells; *x*, supporting cell of Deiters; *w*, nerve-fibre arborising round the first of the external hair-cells; *l l* to *l*, lamina reticularis. × 800. (Waldeyer.)

middle ears are conducting; the internal ear is conducting and receptive. In the external ear the vibrations travel through air; in the middle ear through solid structures—membranes and bones; and in the internal ear through fluid, first through the perilymph on the far side of the fenestra ovalis; and then the vibrations pass through the basilar membrane, and membrane of Reissner, and set the endolymph of the canal of the cochlea in motion.

This is the normal way in which the vibrations pass, but the endolymph may be affected in other ways, for instance through the other bones of the head; one can, for example, hear the ticking of one's watch when it is placed between the teeth, even when the ears are stopped. From this fact is derived a valuable practical method of distinguishing in a deaf person what part of the organ of hearing is at fault. The patient may not be able to hear a watch or a tuning-fork when it is held close to the ear; but if he can hear it when it is placed between his teeth, or on his forehead, the malady is localised in either the external or middle ear; if he can hear it in neither situation, it is a much more serious case, for then the internal ear or the nervous mechanism of hearing is at fault. In disease of the middle ear the hearing of low tones is especially affected; high tones appear to be transmissable by bone-conduction more readily than low.

In connection with the external ear there is not much more to be said; the pinna in many animals is large and acts as a kind of natural ear-trumpet to collect the vibrations of the air; in man this function is to a very great extent lost, and though there are muscles present to move it into appropriate postures, they are not under the control of the will in the majority of people, and are functionless, ancestral vestiges.

In the middle ear, however, there are several points to be considered, namely, the action of the membrana tympani, of the ossicles, of the tympanic muscles, and of the Eustachian tube.

The Membrana Tympani.—This membrane, unlike that of ordinary drums, can take up and vibrate in response to, not only its own fundamental tone, but to an immense range of tones differing from each other by many octaves. This would clearly be impossible if it were an evenly stretched membrane. It is not evenly nor very tightly stretched, but owing to its attachment to the chain of ossicles it is slightly funnel-shaped: the ossicles also damp the continuance of the vibrations.

When the membrane gets too tightly stretched, by increase or decrease of the pressure of the air in the tympanum, then the sense of hearing is dulled. The pressure in the tympanic cavity is kept the same as that of the atmosphere by the *Eustachian tube*, which leads from the cavity to the pharynx, and so to the external air. The Eustachian tube is not, however, always open; it is opened by the action of the *tensor palati* during swallowing. Suppose it were closed owing to swelling of its mucous membrane—this often happens in inflammation of the throat—the result would be what is called *Eustachian* or *throat deafness*, and this is relieved by passing a catheter so as to open the tube. When the tube is closed, an interchange of gases takes place between the imprisoned air and the blood of the tympanic vessels. In time, as in the aërotomometer (see p. 381), equilibrium is established and the tension of the imprisoned gases becomes equal to that of the blood-gases, not to that of the atmosphere. The membrane is therefore cupped inwards by the atmospheric pressure on its exterior; it is this increased tightening of the membrane that produces deafness. There is also an accumulation of mucus. When one makes a violent expiration, as in sneezing, some air is often forced through the Eustachian tube into the tympanum. The ears feel as though they were bulged out, as indeed the membrana tympani is, and there is again partial deafness, which sensations are at once relieved by swallowing so as to open the Eustachian tube and thus re-establish equality of pressure once more.

The ossicles communicate the vibrations of the membrana tympani (to which the handle of the malleus is fixed) to the membrane which closes the fenestra ovalis (to which the foot of the stapes is attached). Thus the vibrations are communicated to the fluid of the internal ear which is situated on the other side of the oval window.

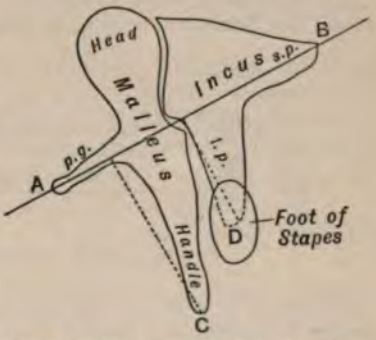

FIG. 549.—Diagrammatic view of ear ossicles.

The accompanying diagram will assist us in understanding how this is brought about. The bones all vibrate as if they were one, the slight movements between the individual bones being inappreciable. The utility of there being several bones is seen when the vibrations are excessive; the small amount of "give" at the articulations is really protective and tends to prevent fractures.

The handle of the malleus is inserted between the layers of the tympanic membrane; the processus gracilis (*p. g.*) has its end A attached to the tympanic wall on the inner aspect of the Glaserian fissure; the end B of the short process (*s. p.*) of the incus is fastened by a ligament to the opposite wall of the tympanic cavity; the end D of the long process of the incus articulates with the stirrup, the base of which is turned towards the reader. The handle vibrates with the membrana tympani; and the vibrations of the whole chain take place round the *axis of rotation* AB. Every time C comes forwards D comes forwards, but by drawing perpendiculars from C and D to the axis of rotation, it is found that D is about $\frac{2}{3}$ of the distance from the axis that C is. So in the transmission of the vibrations from membrane to membrane across the bony chain, the amplitude of the vibration is decreased by about $\frac{1}{3}$, and the force is correspondingly increased. This increase of power is augmented by the fact that the tympanic membrane concentrates its power upon an area (the membrane of the oval window) only one-twentieth of its size. The final movement of the stapes is, however, always very small; it varies from $\frac{1}{15}$ to less than $\frac{1}{10000}$ of a millimetre.

The action of the *tensor tympani*, by pulling in the handle of the malleus, increases the tension of the membrana tympani. It is supplied by the fifth nerve. It is opposed by the strong external ligament of the malleus. The *stapedius* attached to the neck of the stapes tilts it backwards and diminishes the intra-tympanic air-pressure. It is supplied by the seventh nerve.

The next very simple diagram (fig. 550) will explain the use of the *fenestra rotunda.*

The cochlea is supposed to be uncoiled; the scala vestibuli leads from the fenestra ovalis, to the other side of which the stapes is attached; the scala tympani leads to the fenestra rotunda; the two scalæ communicate at the helicotrema, and are separated from the canal of the cochlea by the basilar membrane, and the membrane of Reissner. C.R. is the canalis reuniens leading to the saccule. The cochlea is filled with incompressible fluid in an inexpansible bony case, except where the windows are closed by membranes. Hence every time the membrane of the oval window is bulged in by the stirrup, the membrane of the round window is simultaneously bulged out to the same extent, and *vice versâ.* These changes of pressure are transmitted from one scala to the other directly through the cochlear canal, setting it into vibration, and through the helicotrema.

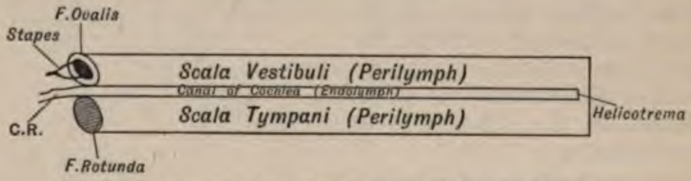
F.Ovalis
Stapes
Scala Vestibuli (Perilymph)
Canal of Cochlea (Endolymph)
Scala Tympani (Perilymph)
Helicotrema
C.R.
F.Rotunda

FIG. 550.—Diagram to illustrate the use of the fenestra rotunda.

The range of hearing extends over 10 or 11 octaves; the lowest audible tone having about 20, the highest about 25,000, vibrations per second. The range varies in different people, and diminishes from childhood onwards. The upper limit of hearing may be tested by minute forks, metal rods, or by Galton's whistle. Many animals appear to be able to detect high tones which lie beyond the human limit. The lower limit may be determined by very large forks, or by employing very low difference-tones.

Difference-tones are produced when two tones of different pitch, *m* and *n*, are sounded together. A tone having the pitch *m* minus *n* is then heard in addition to the tones *m* and *n*: also a summation tone of pitch *m* plus *n* may be heard, but with greater difficulty. When *m* and *n* are nearly equal, a beating tone, instead of a difference-tone, results, having a pitch somewhere intermediate between *m* and *n*. If the difference between *m* and *n* is exceedingly small, this beating-tone alone is heard. The frequency of the beats corresponds to the difference in vibration-rates, *m* and *n*. Under certain conditions the difference and summation-tones (which are collectively called combination-tones) exist in the air; their presence being demonstrable by their re-inforcement before appropriate resonators. More generally, however, they appear to be produced within the ear, *i.e.*, they have merely a subjective origin.

The smallest perceptible difference in pitch between two successive tones is about 0·2 vibrations in the middle region of the piano for trained subjects. Practice effects extraordinary improvement, even among the most unmusical.

There can be little doubt that the cochlea is the organ specially concerned in hearing. It first appears among vertebrata in certain fishes as a very rudimentary structure. If the cochlea is removed from dogs, they become deaf. The utricle and saccule are probably only stimulated by gross disturbances in the surrounding media (see the functions of the semicircular canals in Chapter XLIX.).

There are two classes of theories of hearing, in both of which the basilar membrane of the cochlea plays the essential part.

The one class comprises the many "sound-picture" theories which have been advanced in very various forms by Rutherford, Waller, Hurst, Ewald, and Meyer. The entire basilar membrane is supposed to vibrate either as a telephone plate, or as an elastic membrane, different tones or combinations of tones giving rise to different patterns of vibrations which are communicated to the hair-cells and thence carried by the auditory nerve-fibres to the brain, where (in Rutherford's theory) the analysis of these patterns is held to take place.

The other is the resonance-theory of Helmholtz, in which the pitch of a tone, or the analysis of a complex sound into its constituent tones, is determined not in the brain but in the cochlea. It depends on the principle of sympathetic vibration. As is well known, if a tone is sung in front of a piano (best with the loud pedal held down), the string of the piano which is attuned to that tone will immediately respond; another tone will elicit response from another string. So in the cochlea the appropriate fibre of the basilar membrane is thrown into vibration when the tone to which it is attuned reaches it. The fibre thus stimulated affects the hair-cells above it, whence the stimulus is conducted to the brain. If two tones are sounded together, the two appropriate fibres respond, and the analysis of the now more complex stimulus is performed in the cochlea. The fibres of the basilar membrane increase in radial length from the base towards the apex of the cochlea. According to the resonance-theory, the upper part of the organ would thus be affected by low tones, the lower part by high tones.

The first of these two classes of theory makes it difficult or impossible for us to explain our ability to analyse complex chords into their component tones. The full acceptance of the second is difficult in the face of the small difference of length (at most 1: 12) between the shortest and the longest of the basilar fibres. On the other hand, it accounts for nearly all the phenomena which require explanation, and gains support from the effects of experiment on, and disease of, different portions of the cochlea. For instance, the deafness to high pitched tones (seen in boiler makers) is associated with disease of the lower whorl of the cochlea.

CHAPTER LV

VOICE AND SPEECH

THE fundamental tones of the voice are produced by the current of expired air causing the vibration of the vocal cords, two elastic bands contained in a cartilaginous box placed at the top of the wind-pipe or trachea. This box is called the *larynx*. The sounds produced here are modified by other parts like the tongue, teeth, and lips, as will be explained later on.

Anatomy of the Larynx.

The cartilages of the larynx are the thyroid, the cricoid, the two arytenoids. These are the most important for voice production; they are made of hyaline cartilage. Then there are the epiglottis, two cornicular, and two cuneiform cartilages. These are made of yellow fibro-cartilage.

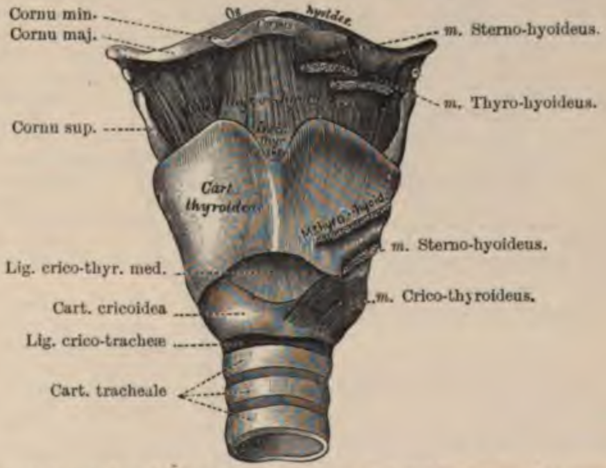

FIG. 551.—The larynx, as seen from the front showing the cartilages and ligaments. The muscles, with the exception of one crico-thyroid, are cut off short. (Stoerk.)

The *thyroid* cartilage (fig. 552, 1 to 4) does not form a complete ring around the larynx, but only covers the front portion. It forms the prominence in front of the throat known as Adam's apple. The *cricoid* cartilage (fig. 552, 5, 6), on the other hand, is a complete ring; the back part of the ring is much broader than the front. On the top of this broad portion of the cricoid are the *arytenoid* cartilages (fig. 552, 7); the connection between the cricoid below and arytenoid cartilages above is a joint with synovial membrane and ligaments, the latter permitting tolerably free motion between them. But although the arytenoid cartilages can move on the cricoid, they accompany the latter in all its movements. The base by means of which each arytenoid cartilage sits on the cricoid is triangular; the anterior angle is often called the vocal process: to it the posterior ends of the true vocal cords are attached. The outer angle is thick and called the muscular process.

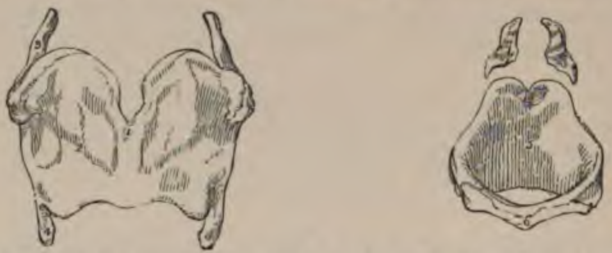

FIG. 552.—Cartilages of the larynx seen from the front. 1 to 4, Thyroid cartilage; 1, vertical ridge or pomum Adami; 2, right ala; 3, superior, and 4, inferior cornu of the right side; 5, 6, cricoid cartilage; 5, inside of the posterior part; 6, anterior narrow part of the ring; 7, arytenoid cartilages. × ¾.

The cornicular cartilages, or cartilages of Santorini, are perched on the top of the arytenoids; the cuneiform cartilages, or cartilages of Wrisberg, are in a fold of mucous membrane; the epiglottis looks like a lid to the whole (fig. 553).

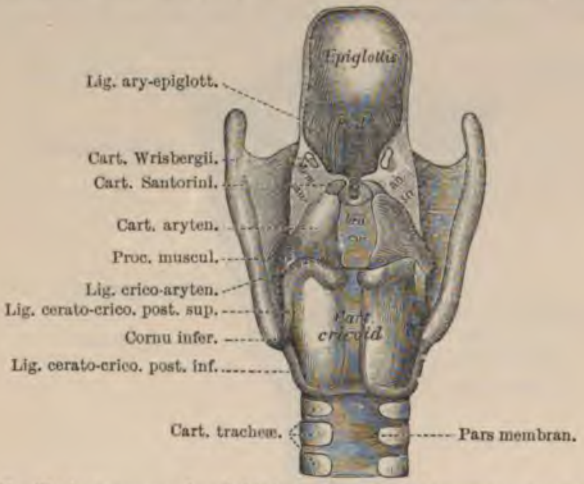

FIG. 553.—The larynx as seen from behind after removal of the muscles. The cartilages and ligaments only remain. (Stoerk.)

The thyroid cartilage is connected with the cricoid, by the crico-thyroid membrane, and also by joints with synovial membranes; the lower *cornua* of the thyroid clasp the cricoid between them, yet not so tightly but that the thyroid can revolve, within a certain range, around an axis passing transversely through the two joints at which the cricoid is clasped. The vocal cords are attached behind to the front portion of the base (vocal process) of the arytenoid cartilages, and in front to the re-entering angle at the back of the thyroid; it is evident, therefore, that all movements of either of these cartilages must produce an effect on them of some kind or other. Inasmuch, too, as the arytenoid cartilages rest on the top of the back portion of the cricoid cartilage, and are connected with it by capsular and other ligaments, all movements of the cricoid cartilage must move the arytenoid cartilages, and also produce an effect on the vocal cords.

Mucous membrane.—The larynx is lined with a mucous membrane continuous with that of the trachea; this is covered with ciliated epithelium except over the vocal cords and epiglottis, where it is stratified. The vocal cords are thickened bands of elastic tissue in this mucous membrane which run from before back. They are attached behind to the vocal processes of the arytenoid cartilages, and in front to the angle where the two wings of the thyroid meet. The chink between them is called the *rima glottidis* (see fig. 554). Two ridges of mucous membrane above and parallel to these are called the *false vocal cords;* between the true and false vocal cord on each side is a recess called the *ventricle.*

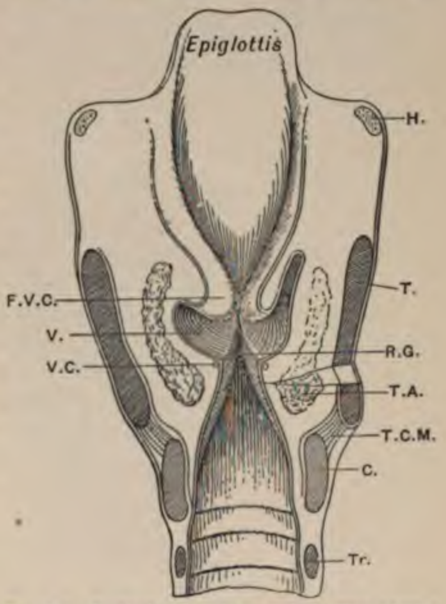

Fig. 554.—Vertical section through the larynx, passing from side to side. H, Hyoid bone; T., thyroid cartilage; T.C.M., thyro-cricoid membrane; C., cricoid cartilage; Tr., first ring of trachea; T.A., thyro-arytenoid muscle; R.G., rima glottidis; V.C., vocal cord; V., ventricle; F.V.C., false vocal cord. (After Allen Thomson.)

Muscles.—The muscles of the larynx are divided into intrinsic and extrinsic. The intrinsic are named from their attachments to the various cartilages; the extrinsic are those which connect the larynx to other parts like the hyoid bone.

The intrinsic muscles of the larynx are as follows:—

1. Crico-thyroid.
2. Posterior crico-arytenoid.
3. Lateral crico-arytenoid.
4. Thyro-arytenoid.
5. Arytenoid.

All these muscles except the arytenoid are in pairs.

Their attachments and actions are as follows:—

1. *Crico-thyroid.*—This is a short, thick triangular muscle, attached below to the cricoid cartilage; this attachment extends from the middle line backwards. The fibres pass upwards and outwards, diverging slightly to be attached above to the inferior border of the thyroid cartilage, and to the anterior border of its lower cornu. In the latter portion of the muscle, the fibres are nearly horizontal. Some of the superficial fibres are continuous with those of the inferior constrictor of the pharynx.

The thyroid cartilage being fixed by extrinsic muscles, the contraction of this muscle draws upwards the anterior part of the cricoid cartilage, and depresses the posterior part, and with it the arytenoid cartilages, so that the vocal cords are stretched. Paralysis of these muscles therefore causes an inability to produce high-pitched tones.

2. *Posterior crico-arytenoid.*—This arises from the broad depression on the corresponding half of the posterior surface of the cricoid cartilage; its fibres con-

verge upwards and outwards, and are inserted into the outer angle of the base of the arytenoid cartilage behind the attachment of the lateral crico-arytenoid muscle. Near their insertion the upper fibres are blended with the lower fibres of the arytenoid muscle.

These muscles draw the outer angles of the arytenoid cartilages backwards and inwards, and thus rotate the anterior or vocal processes outwards, and widen the rima glottidis. They come into action during deep inspiration. If they are paralysed, the lips of the glottis approach the middle line and come in contact during each inspiration, so that dyspnœa is produced.

3. *Lateral crico-arytenoid.*—This arises from the sloping upper border of the cricoid cartilage, and is inserted into the muscular process of the arytenoid cartilage, and the adjacent part of its anterior surface. Its upper part is more or less blended with the thyro-arytenoid, and a few of its fibres are continuous round the outer side of the arytenoid cartilage with the arytenoid muscle.

These muscles draw the muscular processes of the arytenoid cartilages forwards and downwards, and thus approximate the vocal cords. They are antagonistic to the posterior crico-arytenoids.

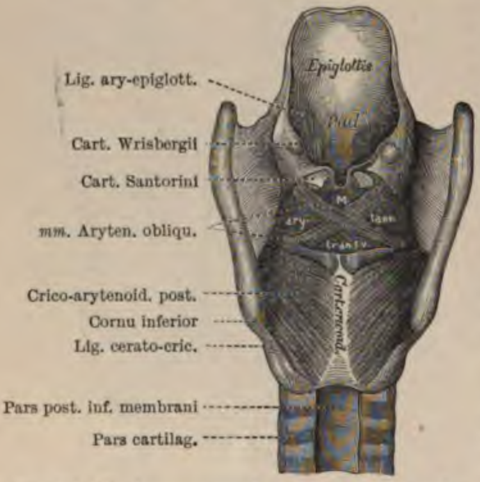

FIG. 555.—The larynx as seen from behind. To show the intrinsic muscles posteriorly. (Stoerk.)

4. *Thyro-arytenoid.* — This consists of two portions, inner and outer. The *inner* portion arises in the lower half of the angle formed by the alæ of the thyroid cartilage, and passing backwards is attached behind to the vocal process and to the adjacent parts of the outer surface of the arytenoid cartilage. These fibres are joined internally by short fibres which are attached in front to the vocal cord, and behind to the vocal process. Some oblique fibres pass from the sloping portion of the crico-thyroid membrane below the vocal cord, upwards, outwards, and somewhat backwards, to end in the tissue of the false vocal cord. The fibres of the *outer* portion arise in front from the thyroid cartilage close to the origin of the inner portion and from the crico-thyroid membrane. They pass backwards to be inserted in part into the lateral border and muscular process of the arytenoid cartilage, and in part they pass obliquely upwards towards the aryteno-epiglottidean fold, ending in the false vocal cord. The portion of this muscle which extends towards the epiglottis is often described as a separate muscle (*thyro-epiglottidean*); it resembles the crico-arytenoid in that some of its fibres are continuous with those of the arytenoid muscle.

The antero-posterior fibres will tend to draw forward the arytenoid cartilage, and with it the posterior part of the cricoid cartilage, rotating the latter upwards and antagonising the action of the crico-thyroid muscle, the effect being to relax the vocal cords. But if the latter are kept stretched those fibres of the inner portion of the muscle which are inserted into the vocal cord may serve to modify its elasticity, tightening the parts of the cord in front of, and relaxing those behind, its attachment. The vertical fibres of the muscle which extend from the crico-thyroid membrane across the base of the vocal fold and over the ventricle into the false vocal cord, render the free edge of the former more prominent. Then the fibres which are inserted into the muscular process and outer surface of the arytenoid cartilage will tend to draw the arytenoid cartilage forwards and rotate it inwards; finally, the fibres which pass into the aryteno-epiglottidean fold may assist in depressing the epiglottis.

If these muscles are paralysed, the lips of the glottis are no longer parallel, but are curved with the concavity inwards, and a much stronger blast of air is required for the production of the voice.

5. *Arytenoid.*—When the mucous membrane is removed from the back of the arytenoid cartilages, a band of transverse fibres is exposed, on the dorsal surface of which are two slender decussating oblique bundles. These are often described as separate muscles (arytenoid and aryteno-epiglottidean), but they are intimately blended together. The ventral fibres (arytenoid proper) pass straight across from the outer half of the concave surface on the back of one arytenoid cartilage to the corresponding surface of the other. The dorsal fibres can be followed to the lateral walls of the larynx, the uppermost ones to the cartilage of Santorini, the intermediate ones run with the uppermost fibres of the thyro-arytenoid muscle forming the so-called aryteno-epiglottidean muscle, and the lowest fibres blend at the level of the true vocal cords with the thyro-arytenoid and lateral crico-arytenoid muscles.

The arytenoid muscle draws the arytenoid cartilages together. If it is paralysed, the intercartilaginous part of the glottis remains open, although the membranous lips can still be approximated during vocalisation.

It has been generally supposed that the epiglottis is depressed as a lid over the glottis during swallowing. This may be so in some animals, but in man it is not the case; the epiglottis projects upwards in close contact with the base of the tongue. The necessary closure of the glottis during swallowing is brought about by the contraction of the arytenoid and thyro-arytenoid muscles; by this means the arytenoid cartilages are drawn towards each other, and also forwards into contact with the posterior surface of the epiglottis (Anderson Stuart). Henle remarks that "the muscles which lie in the space enclosed by the laminæ of the thyroid cartilage and above the cricoid may be regarded in their totality as a kind of sphincter such as is found in its simplest form embracing the entrance of the larynx in reptiles" (Quain's Anatomy).

Nerves.—The larynx is supplied by two branches of the vagus; the *superior laryngeal* is the sensory nerve; by its *external* branch, it supplies one muscle, namely, the crico-thyroid. These fibres, however, probably arise from glosso-pharyngeal rootlets (see p. 645). The rest of the muscles are supplied by the *inferior laryngeal nerve*, the fibres of which come from the spinal accessory, not the vagus proper.

The laryngoscope is an instrument employed in investigating during life the condition of the pharynx, larynx, and trachea. It consists of a large concave mirror with perforated centre, and of a smaller mirror fixed in a long handle. The patient is placed in a chair, a good light (argand burner, or electric lamp) is arranged on one side of, and a little above, his head. The operator fixes the large mirror round his head in such a manner, that he looks through the central aperture with one eye He then seats himself opposite the patient, and so alters the position of the mirror, which is for this purpose provided with a ball-and-socket joint, that a beam of light is reflected on the lips of the patient.

The patient is now directed to throw his head slightly backwards, and to open his mouth; the reflection from the mirror lights up the cavity of the mouth, and by a little alteration of the distance between the operator and the patient the point at which the greatest amount of light is reflected by the mirror—in other words, its focal length—is readily discovered. The small mirror fixed in the handle is then warmed, either by holding it over the lamp, or by putting it into a vessel of warm water; this is necessary to prevent the condensation of breath upon its surface. The degree of heat is regulated by applying the back of the mirror to the hand or cheek, when it should feel warm without being painful.

After these preliminaries the patient is directed to put out his tongue, which is held by the left hand gently but firmly against the lower teeth by means of a handkerchief. The warm mirror is passed to the back of the mouth, until it rests upon and slightly raises the base of the uvula, and at the same time the light is directed upon it: an inverted image of the larynx and trachea will be seen in the mirror. If the dorsum of the tongue is alone seen, the handle of the mirror must be slightly lowered until the larynx comes into view; care should be taken, however, not to move the mirror upon the uvula, as it excites retching. The observation should not be prolonged, but should rather be repeated at short intervals.

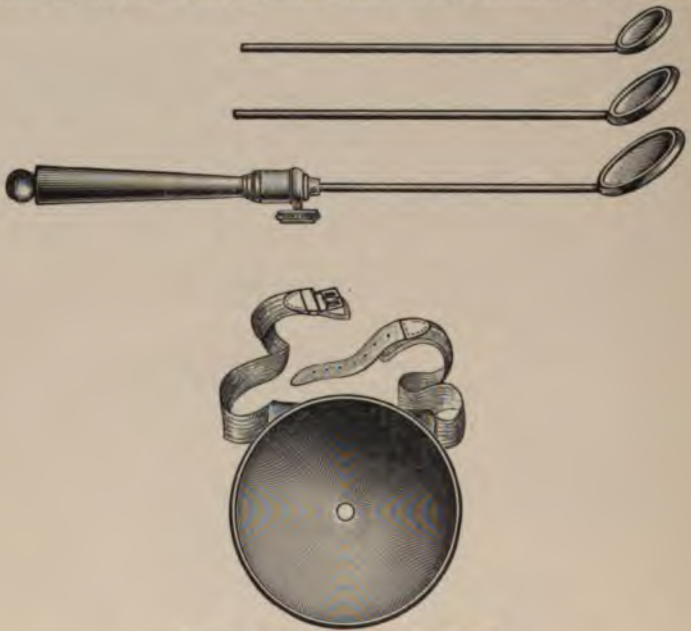

FIG. 556.—The parts of the Laryngoscope.

The structures seen will vary somewhat according to the condition of the parts as to inspiration, expiration, phonation, etc.; they are (fig. 558) first, and apparently at the posterior part, the *base of the tongue*, immediately below which is the arcuate outline of the *epiglottis*, with its cushion or tubercle. Then are seen in the central

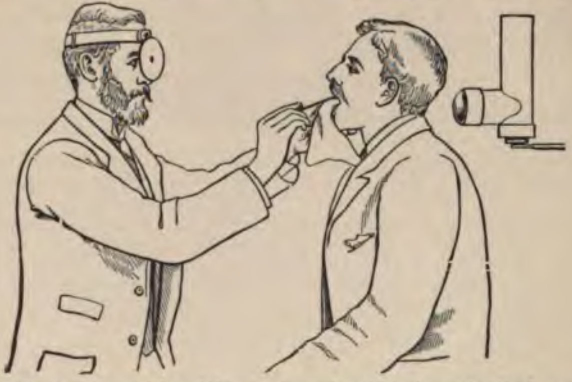

FIG. 557.—To show the position of the operator and patient when using the Laryngoscope.

line the *true vocal cords*, white and shining in their normal condition. The cords approximate (in the inverted image) posteriorly; between them is left a chink, narrow whilst a high note is being sung, wide during a deep inspiration. On each side of the true vocal cords, and on a higher level, are the pink *false vocal cords*. Still more externally than the false vocal cords is the *aryteno-epiglottidean* fold, in which are situated upon each side three small elevations; of these the most external is the *cartilage of Wrisberg*, the intermediate is the *cartilage of Santorini*, whilst the summit of the *arytenoid cartilage* is in front, and somewhat below the preceding, being only seen during deep inspiration. The *rings of the trachea*, and even the bifurcation of the trachea itself, if the patient be directed to draw a deep breath, may be seen in the interval between the true vocal cords.

Movements of the Vocal Cords.

In Respiration.—The position of the vocal cords in ordinary tranquil breathing is so adapted by the muscles, that the opening of the glottis is wide and triangular (fig. 558, B). For all practical purposes, the glottis remains unaltered during ordinary quiet breathing, though in a small proportion of people it becomes a little wider at each inspiration, and a little narrower at each expiration. In the cadaveric position the glottis has about half the width it has during ordinary breathing; during life, therefore, except during vocalisation, the abductors of the vocal cords (posterior crico-arytenoids) are in constant action. (F. Semon.) On making a rapid and deep inspiration the opening of the glottis is widely dilated (fig. 558, C), and somewhat lozenge-shaped.

In Vocalisation.—At the moment of the emission of a note, the chink is narrowed, the margins of the arytenoid cartilages being brought into contact, and the edges of the vocal cords approximated and made parallel (fig. 558, A); at the same time their tension is much increased. The higher the note produced, the tenser do the cords become; and the range of a voice depends, in the main, on the extent to which the degree of tension of the vocal cords can be thus altered. In the production of a high note the vocal cords are brought well within sight, so as to be plainly visible with the help of the laryngoscope. In the utterance of low-pitched tones, on the other hand, the epiglottis is depressed and brought over them, and the arytenoid cartilages look as if they were trying to hide themselves under it (fig. 559). The epiglottis, by being somewhat pressed down so as to cover the superior cavity of the larynx, serves to render the notes deeper in tone and at the same time somewhat duller.

The degree of approximation of the vocal cords also usually corresponds with the height of the note produced; but the width of the aperture has no essential influence on the pitch of the note, as long as the vocal cords have the same tension: only with a wide aperture the tone is more difficult to produce and is less perfect, the rushing of the air through the aperture being heard at the same time.

No true vocal sound is produced at the posterior part of the aperture of the glottis, that, viz., which is formed by the space between the arytenoid cartilages.

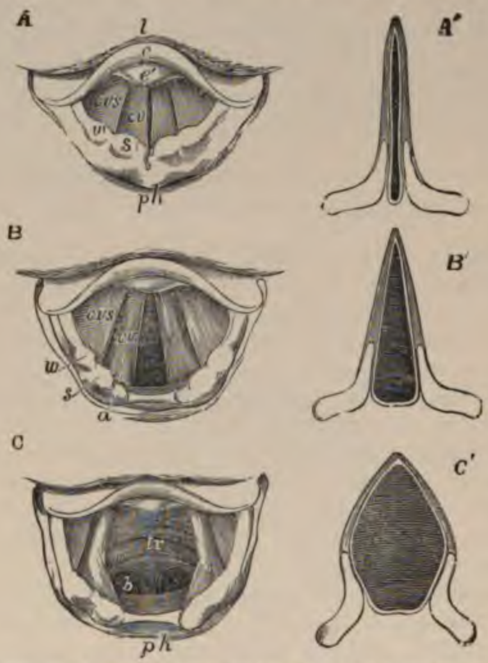

FIG. 558.—Three laryngoscopic views of the superior aperture of the larynx and surrounding parts. A, The glottis during the emission of a high note in singing; B, in easy and quiet inhalation of air; C, in the state of widest possible dilatation, as in inhaling a very deep breath. The diagrams A′, B′, and C′, show in horizontal sections of the glottis the position of the vocal cords and arytenoid cartilages in the three several states represented in the other figures. In all the figures so far as marked, the letters indicate the parts as follows, viz.: *l*, the base of the tongue; *e*, the upper free part of the epiglottis; *e′*, the tubercle or cushion of the epiglottis; *ph*, part of the anterior wall of the pharynx behind the larynx; in the margin of the aryteno-epiglottidean fold, *w*, the swelling of the membrane caused by the cartilages of Wrisberg; *s*, that of the cartilages of Santorini; *a*, the tip or summit of the arytenoid cartilages; *c v*, the true vocal cords or lips of the rima glottidis; *c v s*, the superior or false vocal cords; between them the ventricle of the larynx; in C, *tr* is placed on the anterior wall of the receding trachea, and *b* indicates the commencement of the two bronchi beyond the bifurcation which may be brought into view in this state of extreme dilatation. (Quain, after Czermak.)

The Voice.

The human musical instrument is often compared to a reed organ-pipe: certainly the notes produced by such pipes in the *vox humana* stop of organs is very like the human voice. Here there is not only the vibration of a column of air, but also of a reed, which corresponds to the vocal cords in the air-chamber composed of the trachea and the bronchial system beneath it. The pharynx, mouth, and nasal cavities above the glottis are resonating cavities, which, by alterations in their shape and size, are able to pick out and emphasize certain component parts of the fundamental tones produced in the larynx. The natural voice is often called the *chest voice.* The *falsetto voice* is differently explained by different observers; on laryngoscopic examination, the glottis is found to be widely open, so that there is an absence of chest resonance; some have supposed that the attachment of the thyro-arytenoid muscle to the vocal cord renders it capable of acting like the finger on a violin string, part of the cord being allowed to vibrate while the rest is held still. Such a shortening of a vibrating string would produce a higher pitched note than is natural.

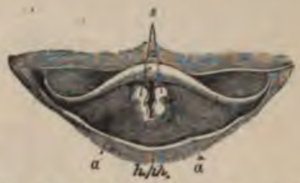

Fig. 559.—View of the upper part of the larynx as seen by means of the laryngoscope during the utterance of a bass note. *e*, Epiglottis; *s*, tubercles of the cartilages of Santorini; *a*, arytenoid cartilages; *z*, base of the tongue; *ph*, the posterior wall of the pharynx. (Czermak.)

Musical sounds differ from one another in three ways:—

1. *In pitch.*—This depends on the rate of vibration; and in the case of a string, the pitch increases with the tension, and diminishes with the length of the string. The vocal cords of a woman are shorter than those of a man, hence the higher pitched voice of women. The average length of the female cord is 11·5 millimetres; this can be stretched to 14; the male cord averages 15·5, and can be stretched to 19·5 millimetres.

2. *In loudness.*—This depends on the amplitude of the vibrations, and is increased by the force of the expiratory blast which sets the cords in motion.

3. *In "timbre."*—This is the difference of character which distinguishes one voice, or one musical instrument, from another. It is due to admixture of the primary vibrations with secondary vibrations or overtones. If one takes a tracing of a tuning-fork on a revolving cylinder, it writes a simple series of up and down waves corresponding in rate to the note of the fork. Other musical instruments do not lend themselves to this form of graphic record, but their vibrations can be rendered visible by allowing them to act on a small sensitive gas-flame; this bobs up and down, and if the reflection of this flame is allowed to fall on a series of mirrors, the top of the continuous image formed is seen to present waves. The mirrors are usually arranged on the four lateral sides of a cube which is rapidly rotated. If one sings a note on to the membrane in the side of the gas-chamber with which the flame is in connection, the waves seen are not simple up and down ones, but the primary large waves are

complicated by smaller ones on their surface, at twice, thrice, etc., the rate of the primary vibration. The richer a voice, the richer the sound of a musical instrument, the more numerous are these overtones or harmonics.

The range of the voice is seldom, except in celebrated singers, more than two-and-a-half octaves, and for different voices this is in different parts of the musical scale.

Although the voice is usually produced by the expiratory blast, by practice one can employ the inspiratory blast; this constitutes the form of speech known as *ventriloquism.* The voice does not appear to come out of the speaker's mouth; and as we never readily distinguish the direction in which the sounds reach our ear, the ventriloquist, by directing the attention of the audience to various parts of the room, is able to make them imagine the voice is proceeding from those parts.

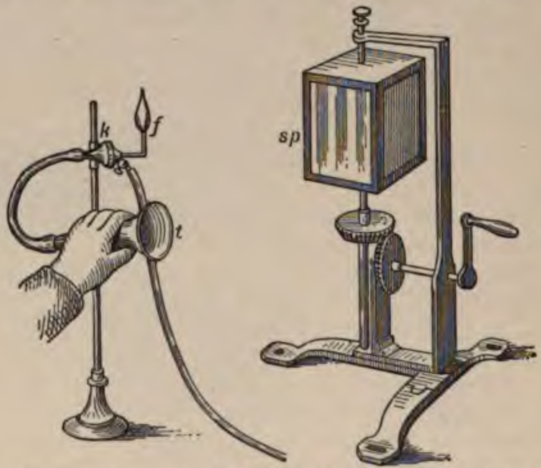

FIG. 560.—König's apparatus for obtaining flame pictures of musical notes.

Speech.

This is due to the modification produced in the fundamental laryngeal notes, by the resonating cavities above the vocal cords. By modifying the size and shape of the pharynx, mouth, and nose, certain overtones or harmonics are picked out and exaggerated: this gives us the vowel sounds; the consonants are produced by interruptions, more or less complete, of the outflowing air in different situations. The soft palate is raised at each word. When the larynx is passive, and the resonating cavities alone come into play, then we get whispering.

The pitch of the **Vowels** has been estimated musically; *u* has the lowest pitch, then *o*, *a* (as in father), *a* (as in cane), *i*, and *e*. We may give a few examples of the shape of the resonating cavities in pronouncing vowel sounds, and producing their characteristic timbre: when sounding *a* (in father) the mouth has the shape of a funnel wide in front; the tongue lies on the floor of the mouth; the lips are wide open; the soft palate is moderately and the larynx slightly raised.

In pronouncing *u* (*oo*), the cavity of the mouth is shaped like a capacious flask with a short narrow neck. The whole resonating cavity is then longest, the lips being protruded as far as possible; the larynx is depressed and the root of the tongue approaches the fauces.

In pronouncing *o*, the neck of the flask is shorter and wider, the lips being nearer the teeth; the larynx is slightly higher than in sounding *oo*.

In pronouncing *e*, the flask is a small one with a long narrow neck. The resonating chamber is then shortest as the larynx is raised as much as possible, and the mouth is bounded by the teeth, the lips being retracted; the approach of the tongue near the hard palate makes the long neck of the flask.

The **Consonants** are produced by a more or less complete closure of certain doors on the course of the outgoing blast. If the closure is complete, and the blast suddenly opens the door, the result is an *explosive*; if the door is partly closed, and the air rushes with a hiss through it, the result is an *aspirate*; if the door is nearly closed and its margins are thrown into vibration, the result is a *vibrative*; if the mouth is closed, and the sound has to find its way out through the nose, the result is a *resonant*.

These doors are four in number; Brücke called them the ***articulation positions.*** They are—

1. Between the lips.
2. Between the tongue and hard palate.
3. Between the tongue and soft palate.
4. Between the vocal cords.

The following table classifies the principal consonants according to this plan:—

Articulation position.	Explosives.	Aspirates.	Vibratives.	Resonants.
1	B, P.	F, V, W.	...	M.
2	T, D.	S, Z, L, Sch, Th.	R.	N.
3	K, G.	J, Ch.	Palatal R.	Ng.
4	...	H.	R of lower Saxon	...

The introduction of the phonograph has furnished us with an instrument which it is hoped in the future will enable us to state more accurately than has hitherto been possible, the meaning of the changes in nature and intensity of the complex vibrations which constitute speech. The microscopic study of the tracing on the recording phonographic cylinder, and various methods of obtaining a high magnification of the movements of the recording style have been carried out by M'Kendrick and others. The subject is, however, not yet sufficiently ripe for definite statements to be made.

Defects of Speech.

Speech may be absent in certain forms of lunacy, and temporarily in that defect of will called *hysteria*.

It may be absent owing to congenital defects. Children born deaf are dumb also. This is because we think with remembered sounds, and in a person born deaf the auditory centres are never set into activity. By educating the child by the visual inlet, it can be taught to think with the remembered shapes of the mouth and expressions of the face produced in the act of speaking, and so can itself speak in time.

If a child becomes deaf before it is six or seven years old, there is a liability it will forget the speech it has learnt, and so become dumb.

In congenital hemiplegia there may be speechlessness, especially if the injury is due to meningeal hæmorrhage affecting the grey cortex of the left hemisphere. These children generally talk late, the right side of the brain taking on the function of the left.

Disorders of speech and voice occur from affections of the larynx, and of the nerves which supply the larynx. Stammering is a want of co-ordination between the various muscles employed in the act of speaking.

Perhaps the most interesting of the disorders of speech, however, are those due to brain disease in adults. These fall into three principal categories :—

1. *Aphemia.*—A difficulty or inability to utter or articulate words. It is often associated with difficulty of swallowing, and occurs in lesions of the base of the brain, especially of pons and bulb. The blurring of speech noticed in most cases of apoplexy may also be included under this head.

2. *Aphasia.*—This is a complex condition in which the will to speak exists, and also the ability to speak, but the connection between the two is broken down. When the patient speaks, the words which he utters are well pronounced, but are not those he wishes to utter. This is often associated with *Agraphia*, a similar condition in respect to writing. It is the form of disordered speech associated with disorganisation of Broca's convolution.

3. *Amnesia.*—This term includes a large class of cases in which the main symptom is loss of memory for words, or a defect of the association of ideas of things with ideas of words, not, as in aphasia, with ideas of verbal action. Amnesia is associated with lesions of the intellectual, *i.e.*, the sensory centres of the cortex behind the Rolandic area. We have seen that in this region of the brain there are two important centres, the visual and the auditory, and the parts of these which are associated with words may be called the *visual word-centre* and the *auditory word-centre.* In amnesia (sometimes called sensory aphasia), either these centres themselves, or the tracts that connect them, are diseased or broken down. See also p. 695.

With regard to the auditory word-centre, impressions for the sounds of words are revived in one of three ways :—

a. Spontaneous or volitional; owing to accumulated traces which constitute memory, a man when he wants to express his thoughts in words remembers the sounds it is necessary to use; impulses pass to the motor-centre (Broca's convolution), thence to the nerve-centres, nerves, and muscles of the larynx, mouth, chest, etc., and the man speaks.

b. In slight disease of the auditory word-centre, he is unable to do this, but if his mind is set into a certain groove he will speak; thus if the alphabet or a well-known piece of poetry be started for him he will finish it by himself.

c. Mimetic. In more severe cases, a more powerful stimulus still is needed; he will repeat any words after another person, but forget them immediately afterwards.

With regard to the visual word-centre as tested by writing, there are also three ways of reviving impressions for written words or letters.

(*a*) Spontaneous or normal.

(*b*) A train of thought must first be set going; as, for instance, converting printed words into written characters.

(*c*) Mimetic; he can only write from a copy.

Two operations require the combined activity of both centres; the first of these is reading aloud, the second is writing from dictation. These, however, we have previously considered in connection with the subject of association in the brain (see p. 695).

In the investigation of any case of defective speech there are always the following six things to be inquired into :—

1. Can the patient understand spoken words? (The patient, of course, not being deaf.) If he cannot, the auditory word-centre is deranged.

2. Can he repeat words when requested? This tests the emission fibres from the auditory word-centre which pass through the motor-centres for speech in Broca's convolution. If he cannot do this, the patient has aphasia.

3. Can he write from dictation? If he cannot, either the auditory or visual word-centre, or the fibres passing from the one to the other, are injured.

4. Does he understand printed matter, and can he point out printed letters and words? Can he read to himself? (The patient, of course, not being blind.) This tests the visual word-centre.

5. Can he copy written words? This tests the channels from the visual word-centre to the motor-centres for movements of the hand in writing.

6. Can he read aloud, or, what is the same thing, name objects he sees? This is the opposite to writing from dictation, and tests the healthiness of the word-centres or the fibres which connect the visual to the auditory word-centre.

CHAPTER LVI

THE EYE AND VISION

THE eyeball is contained in the cavity of the skull called the orbit; here also are vessels and nerves for the supply of the eyeball, muscles to move it, and a quantity of adipose tissue. In the front of the eyeball are the lids and lacrimal apparatus.

The *eyelids* consist of two movable folds of skin, each of which is kept in shape by a thin plate of fibrous tissue called the *tarsus*. Along their free edges are inserted a number of curved hairs (*eyelashes*), which, when the lids are half closed, serve to protect the eye from dust and other foreign bodies: the tactile sensibility of the lids is very delicate. Imbedded in the tarsus are a number of long sebaceous glands (*Meibomian*), the ducts of which open near the free edge of the lid. In the loose connective tissue in front of the tarsus, the bundles of the orbicularis muscle are situated.

The orbital surface of each lid is lined by a delicate, highly sensitive mucous membrane (*conjunctiva*), which is continuous with the skin at the free edge of each lid, and after lining the inner surface of the eyelid is reflected on to the eyeball, being somewhat loosely adherent to the sclerotic coat. Its epithelium, which is columnar, is continued over the cornea as its anterior epithelium, where it becomes stratified. At the inner edge of the eye the conjunctiva becomes continuous with the mucous lining of the lacrimal sac and duct, which again is continuous with the mucous membrane of the nose.

The eyelids are closed by the contraction of a sphincter muscle (*orbicularis*), supplied by the facial nerve; the upper lid is raised by the *levator palpebræ superioris*, supplied by the third nerve.

The *lacrimal gland*, composed of lobules made up of acini resembling the serous salivary glands, is lodged in the upper and outer angle of the orbit. Its secretion, which issues from several ducts on the inner surface of the upper lid, under ordinary circumstances just suffices to keep the conjunctiva moist. It passes out through two small openings (puncta lacrimalia) near the inner angle of the eye, one in each lid, into the lacrimal sac, and thence along the nasal duct into the inferior meatus of the nose. The excessive secretion poured out under the influence of an irritating vapour or painful emotion overflows the lower lid in the form of tears. The secretory nerves are contained in the lacrimal and subcutaneous malar branches of the fifth nerve, and in the cervical sympathetic.

The Eyeball.

The eyeball (fig. 561) consists of the following structures:—

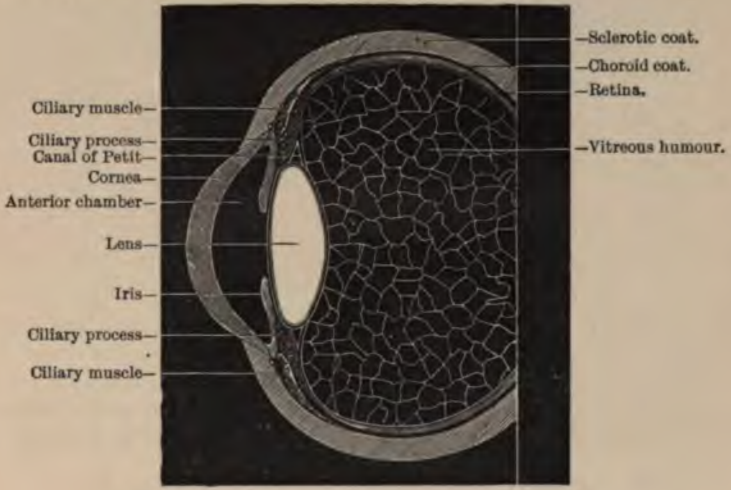

FIG. 561.—Section of the anterior four-fifths of the eyeball.

The *sclerotic*, or outermost coat, envelops about five-sixths of the eyeball: continuous with it, in front, and occupying the remaining sixth, is the *cornea*. Immediately within the sclerotic is the *choroid* coat, and within the choroid is the *retina*. The interior of the

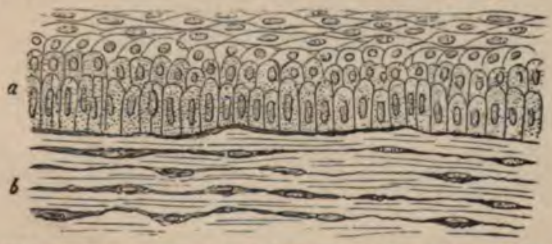

FIG. 562.—Vertical section of rabbit's cornea. *a*, Anterior epithelium, showing the different shapes of the cells at various depths from the free surface; *b*, portion of the substance of cornea. (Klein.)

eyeball is filled by the *aqueous* and *vitreous humours* and the *crystalline lens;* but, also, there is suspended in the interior a contractile and perforated curtain,—the *iris*, for regulating the admission of light, and behind at the junction of the sclerotic and cornea is the ciliary muscle, the function of which is to adapt the eye for seeing objects at various distances.

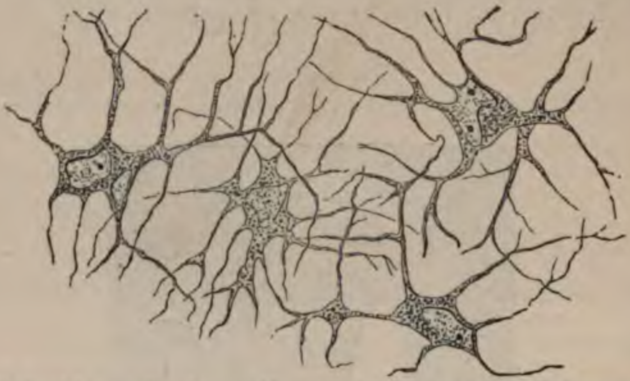

FIG. 563.—Horizontal preparation of cornea of frog; showing the network of branched cornea-corpuscles. The ground substance is completely colourless. × 400. (Klein.)

The sclerotic coat is composed of white fibrous tissue, with some elastic fibres near the inner surface, arranged in variously disposed and interlacing layers. Many of the bundles of fibres cross the others almost at right angles. It is separated from the choroid by a lymphatic space (*perichoroidal*), and this is in connection with smaller spaces lined with endothelium in the sclerotic coat itself. There is a lymphatic space also outside the sclerotic, separating it from a loose investment of connective tissue, containing some smooth

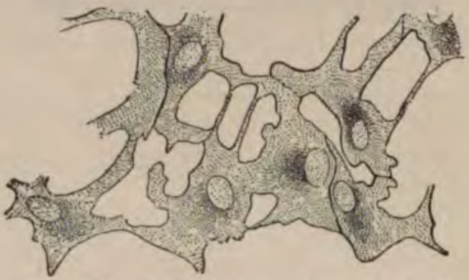

FIG. 564.—Surface view of part of lamella of kitten's cornea, prepared first with caustic potash and then with nitrate of silver. (By this method the branched cornea-corpuscles with their granular protoplasm and large oval nuclei are brought out.) × 450. (Klein and Noble Smith.)

muscular fibres, called the *capsule of Tenon*. The innermost layer of the sclerotic is made up of loose connective tissue and pigment-cells, and is called the *lamina fusca*.

The cornea is a transparent membrane which forms a segment of a smaller sphere than the rest of the eyeball, let in, as it were, into the sclerotic, with which it is continuous all round. It is covered by stratified epithelium (*a*, fig. 562), consisting of seven or eight layers of cells, of which the superficial ones are flattened and scaly, and the deeper ones more or less columnar. Immediately beneath this is the *anterior homogeneous lamina of Bowman*, which differs, only in being more condensed tissue, from the rest of the cornea.

The rest of the cornea consists of many layers of connective tissue fibres arranged parallel to the free surface, the direction of the fibres crossing one another at right angles in the alternate laminæ. The corneal corpuscles lie in branched anastomosing spaces between the laminæ. They have been seen to execute amœboid movements. At its posterior surface the cornea is limited by the *posterior homogeneous lamina*, or *membrane of Descemet*, which is elastic in nature, and lastly a single stratum of cubical epithelial cells (fig. 565, *d*).

The nerves of the cornea are both large and numerous: they are derived from the ciliary nerves. They traverse the substance of the cornea, in which some of them near the anterior surface break up into axis cylinders, and their primitive fibrillæ. The latter form a plexus immediately beneath the epithelium, from which delicate fibrils pass up between the cells anastomosing with horizontal branches, and forming an intra-epithelial plexus. Most of the primitive fibrillæ have a beaded or varicose appearance. The cornea has no blood-vessels or lymphatics, but is nourished by the circulation of lymph in the spaces in which the corneal corpuscles lie. These communicate freely and form a lymph-canalicular system.

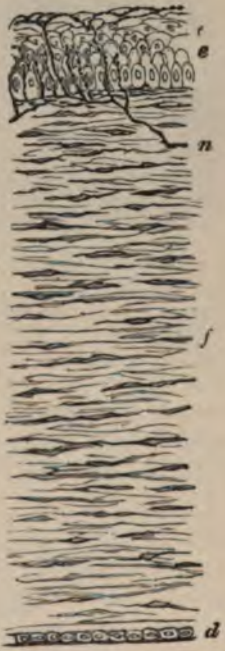

FIG. 565.—Vertical section of rabbit's cornea, stained with gold chloride. *e*, Stratified anterior epithelium. Immediately beneath this is the anterior homogeneous lamina of Bowman. *n*, Nerves forming a delicate sub-epithelial plexus, and sending up fine twigs between the epithelial cells to end in a second plexus on the free surface; *d*, Descemet's membrane, consisting of a fine elastic layer, and a single layer of epithelial cells; the substance of the cornea, *f*, is seen to be fibrillated, and contains many layers of branched corpuscles, arranged parallel to the free surface, and here seen edgewise.

(Schofield.)

The Choroid Coat (*tunica vasculosa*) is attached to the inner layer of the sclerotic in front at the corneo-scleral junction and behind at the entrance of the optic nerve; elsewhere it is connected to it only by loose connective tissue. Its external coat is formed chiefly of elastic fibres and large pigment corpuscles loosely arranged; it contains lymphatic spaces lined with endothelium. This is the *lamina suprachoroidea*. More internally is a layer of arteries and veins arranged in a system of venous whorls, together with elastic fibres and branched pigment cells. The lymphatics, too, are well developed around the blood-vessels, and there are besides distinct lymph spaces lined with endothelium. Internal to this is a layer of fine capillaries, very dense, and derived from the arteries of the outer coat and ending in veins in that coat. It contains corpuscles without pigment, and lymph spaces which surround the blood-vessels (*membrana chorio-capillaris*). It is separated from the retina by a fine elastic membrane (*membrane of Bruch*), which is either structureless or finely fibrillated. (Fig. 566, 1.)

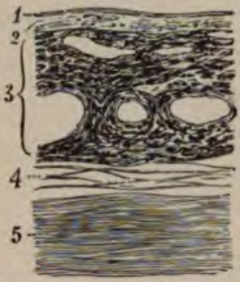

FIG. 566.—Section through the choroid coat of the human eye. 1, Membrane of Bruch; 2, chorio-capillaris or tunica Ruyschiana; 3, proper substance of the choroid with large vessels cut through; 4, suprachoroidea; 5, sclerotic. (Schwalbe.)

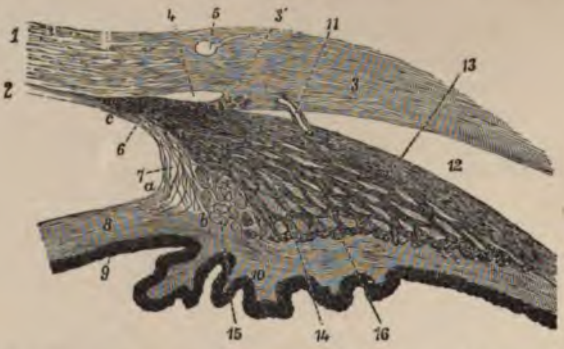

FIG. 567.—Section through the eye carried through the ciliary processes. 1, Cornea; 2, membrane of Descemet; 3, sclerotic; 3', corneo-scleral junction; 4, canal of Schlemm; 5, vein; 6, nucleated network on inner wall of canal of Schlemm; 7, lig. pectinatum iridis, *abc*; 8, iris; 9, pigment of iris (uvea); 10, ciliary processes; 11, ciliary muscle; 12, choroid tissue; 13, meridional, and 14, radiating fibres of ciliary muscle; 15, ring-muscle of Müller; 16, circular or angular bundles of ciliary muscle. (Schwalbe.)

The choroid coat ends in front in what are called the *ciliary processes* (figs. 567, 568). These consist of from 70 to 80 meridionally arranged radiating plaits, which consist of blood-vessels, fibrous connective tissue, and pigment corpuscles. They are lined by a continuation of the membrane of Bruch. The ciliary processes terminate abruptly at the margin of the lens. The *ciliary muscle* (13, 14, and 15, fig. 567), takes origin at the corneo-scleral junction. It is a ring of muscle, 3 mm. broad and 8 mm. thick, made up of fibres running in three directions. (*a*) Meridional fibres near the sclerotic and passing to the choroid; (*b*) radial fibres inserted into the choroid behind the ciliary processes; and (*c*) circular fibres (muscle of Müller), more internal; they constitute a sphincter.

The Iris is a continuation of the choroid inwards beyond the ciliary processes. It is a fibro-muscular membrane perforated by a central aperture, the pupil.

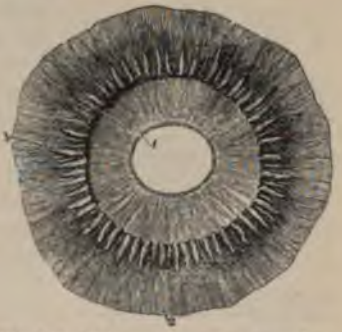

FIG. 568.—Ciliary processes, as seen from behind. 1, Posterior surface of the iris, with the sphincter muscle of the pupil; 2, anterior part of the choroid coat; 3, one of the ciliary processes, of which about seventy are represented.

Posteriorly is a layer of pigment cells (*uvea*), which is a continuation forwards of the pigment layer of the retina. The structure of the iris proper is made of connective tissue in front with corpuscles which may or may not be pigmented, and behind of similar tissue supporting blood-vessels. The pigment cells are usually well developed here, as are also many nerve-fibres radiating towards the pupil. Surrounding the pupil is a layer of circular unstriped muscle, the *sphincter pupillæ*. In some animals there are also muscle-fibres which radiate from the sphincter in the substance of the iris forming the *dilator pupillæ*. The iris is covered anteriorly by a layer of epithelium continued upon it from the posterior surface of the cornea.

The Lens is situated behind the iris, being enclosed in a distinct capsule, the posterior layer of which is not so thick as the anterior. It is supported in place by the suspensory ligament, fused to the anterior surface of the capsule. The suspensory ligament is derived from the hyaloid membrane, which encloses the vitreous humour.

The lens is made up of a series of concentric laminæ (fig. 569), which, when it has been hardened, can be peeled off like the coats of an onion. The laminæ consist of long ribbon-shaped fibres, which in the course of development have originated from cells.

The fibres near the margin have nuclei and are smooth, those near the centre are without nuclei and have serrated edges. They are hexagonal in transverse section. The fibres are united together by a scanty amount of cement substance. The central portion (*nucleus*) of the lens is the hardest.

The epithelium of the lens consists of a layer of cubical cells anteriorly, which merge at the equator into the lens fibres. The development of the lens explains this transition. The lens at first consists of a closed sac composed of a single layer of epithelium. The cells of the posterior part soon elongate forwards and obliterate the cavity; the anterior cells do not grow, but at the edge they become continuous with the posterior cells, which are gradually developed into fibres (fig. 570). The principal chemical constituent of the lens is a proteid of the globulin class called *crystallin*.

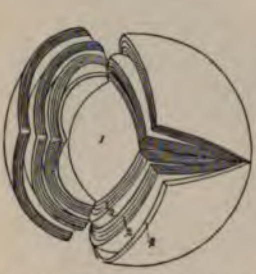

FIG. 569.—Laminated structure of the crystalline lens. The laminæ are split up after hardening in alcohol. 1, The denser central art or nucleus; 2, the successive external layers. ½. (Arnold.)

Corneo-scleral junction.—At this junction the relation of parts (fig. 567) is so important as to need a short description. In this neighbourhood, the iris and ciliary processes join with the cornea. The proper substance of the cornea and the posterior elastic lamina become continuous with the iris, at *the angle of the iris*, and the iris sends forwards processes towards the posterior elastic lamina, forming the *ligamentum pectinatum iridis*, and these join with fibres of the elastic lamina. The epithelial covering of the posterior surface of the cornea is, as we have seen, continuous over the front of the iris. At the iridic angle, the compact inner substance of the cornea is looser, and between the bundles are lymph spaces called the *spaces of Fontana*. They are little developed in the human cornea.

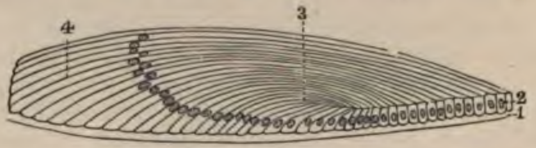

FIG. 570.—Meridional section through the lens of a rabbit. 1, Lens capsule; 2, epithelium of lens; 3, transition of the epithelium into the fibres; 4, lens fibres. (Bubuchin.)

The spaces which are present in the broken-up bundles of corneal tissue at the angle of the iris are continuous with the larger lymphatic space of the anterior chamber. Above the angle at the corneo-scleral junction is a canal, which is called the *canal of Schlemm*. It is a lymphatic channel.

The retina (fig. 571) apparently ends in front, near the outer part of the ciliary processes, in a finely-notched edge,—the *ora* *serrata*, but is really represented by the uvea to the very margin of the pupil. The nerve-cells in the retina remind us that the optic, like the olfactory nerve, is not a mere nerve, but an outgrowth of the brain.

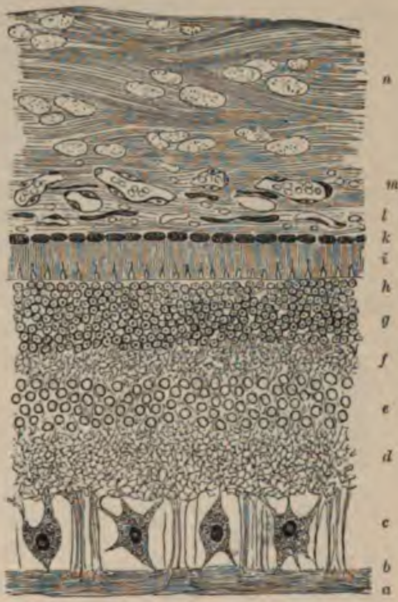

FIG. 571.—A section of the retina, choroid, and part of the sclerotic, moderately magnified; *a*, Membrana limitans interna; *b*, nerve-fibre layer traversed by Müller's sustentacular fibres; *c*, ganglion cell layer; *d*, internal molecular layer; *e*, internal nuclear layer; *f*, external molecular layer; *g*, external nuclear layer; *h*, membrana limitans externa, running along the lower part of *i*, the layer of rods and cones; *k*, pigment cell layer; *l*, *m*, internal and external vascular portions of the choroid, the first containing capillaries, the second larger blood-vessels, cut in transverse section; *n*, sclerotic. (W. Pye.)

In the centre of the retina is a round yellowish elevated spot, about $\frac{1}{24}$ of an inch (1 mm.) in diameter, having a depression in the centre, called after its discoverer the *macula lutea* or *yellow spot of Sœmmering*. The depression in its centre is called the *fovea centralis*. About $\frac{1}{10}$ of an inch (2·5 mm.) to the inner side of the yellow spot, is the point (*optic disc* or *white spot*) at which the optic nerve leaves the eyeball. The optic nerve-fibres are the axons of the nerve-cells of the retina; the dendrons of these cells ultimately communicate with the visual nerve-epithelium (rods and cones).

The optic nerve passes backwards to the ventral surface of the cerebrum enclosed in prolongations of the membranes, which cover the brain. This external sheath at the exit of the nerve from the eyeball becomes continuous with the sclerotic, which at this part is perforated by holes to allow of the passage of the optic nerve-fibres, the perforated part being the *lamina cribrosa*. The pia mater here becomes incomplete, and the subarachnoid and the superarachnoid spaces become continuous. The pia mater sends in processes into the nerve to support the fibres. The fibres of the nerve themselves are exceedingly fine, and are surrounded by the myelin sheath, but do not possess the ordinary external nerve sheath. In the retina itself they have no myelin sheaths. In the centre of the nerve is a small artery, the *arteria centralis retinæ*. The number of fibres in the optic nerve is said to be upwards of 500,000.

The retina consists of certain elements arranged in ten layers from within outwards (figs. 571, 572, 573).

1. *Membrana limitans interna.*—This so-called membrane in contact with the vitreous humour is formed by the junction laterally of the bases of the *sustentacular* or *supporting fibres of Müller*, which bear the same relation to the retina as the neuroglia does to the brain. The character of these fibres may be seen in fig. 572.

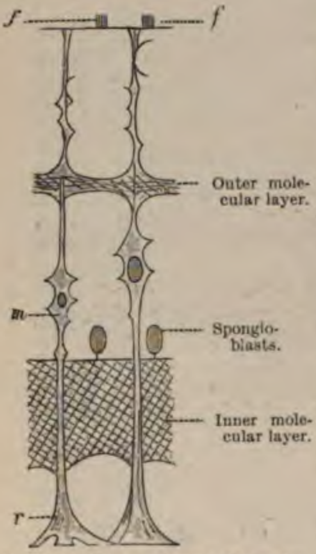

FIG. 572.—Diagram showing the sustentacular fibres of the retina; *f*, fibre-basket above the external limiting membrane; *m*, nucleus of the fibre; *r*, base of the fibre.
(From M'Kendrick, after Stöhr.)

2. *Optic nerve-fibres.*—This layer is of very varying thickness in different parts of the retina: it consists of non-medullated fibres which interlace, and most of which are the axons of the large nerve-cells forming the next layer. The fibres are supported by the sustentacular fibres. They are less and less numerous anteriorly, and end at the ora serrata. They all converge towards the optic disc, where they leave the retina as the optic nerve.

3. *Layer of ganglion cells.*—This consists of large multipolar nerve-cells with large and round nuclei, forming either a single layer, or in some parts of the retina, especially near the *macula lutea*, where this layer is very thick, it consists of several strata of nerve-cells. They are arranged with their single axis-cylinder processes inwards. These pass into and are continuous with the layer of optic nerve-fibres. Externally the cells send off several branched processes which pass into the next layer.

4. *Inner molecular layer.*—This presents a finely granulated appearance. It consists of neuroglia traversed by numerous fibrillar processes of the nerve-cells just described, and the minute branchings of the processes of the bipolar cells of the next layer.

5. *Inner nuclear layer.*—This consists chiefly of numerous small round cells, each with a very small quantity of protoplasm surrounding a large ovoid nucleus; they are generally bipolar, giving off one process outwards and another inwards. One process passes inwards to form a synapse with the arborisation of a ganglion cell, the other outwards to similarly arborise with the branchings of the rod and cone fibres. Some cells, called *spongioblasts*, or *amacrine* cells, however, only send off one process, which passes inwards (fig. 572). The large oval nuclei (fig. 572) belonging to the Müllerian fibres occur in this layer.

6. *Outer molecular layer.*—This layer closely resembles the inner molecular layer, but is much thinner. It contains the branchings of the rod and cone fibres on the one hand and of the bipolar cells on the other.

7. *External nuclear layer.*—This layer consists of small cells resembling at first sight those of the internal nuclear layer; they are classed as rod and cone granules, according as they are connected with the rods and cones respectively, and will be described with them. They are lodged in the meshes of a framework, which is formed by the breaking up of the Müllerian fibres.

8. *Membrana limitans externa.*—This is a well-defined membrane, marking the internal limit of the rod and cone layer, and made up of the junction of the sustentacular fibres externally.

9. *Layer of rods and cones.*—This layer is the nerve-epithelium of the retina. It consists of two kinds of cells, rods and cones, which are arranged at right angles to the external limiting membrane, and supported by hairlike processes (*basket*) proceeding from the latter for a short distance (fig. 572).

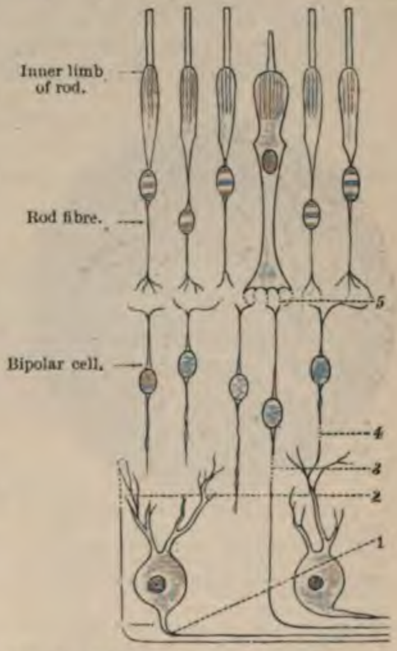

FIG. 573.—Diagram showing the nervous elements of retina. 1, Nerve-fibre of ganglion cell; 2, processes of ganglion cell going outwards; 3, nerve-fibre passing from bipolar cell in inner nuclear layer; 4, process of ganglion cell towards bipolar cell; 5, arborisations of fibres from rods and cones with the branches of bipolar cells.
(From M'Kendrick, after Stöhr.)

Each rod (fig. 573) is made up of two parts, very different in structure, called the outer and inner limbs. The outer limb of the rods is about 30μ long and 2μ broad, is transparent, and doubly refracting. It is said to be made up of fine superimposed discs. It stains brown with osmic acid but not with hæmatoxylin, and resembles in some ways the myelin sheath of a medullated nerve. It is the part of the rod in which the pigment called *visual purple* is found. In some animals, a few rods have a greenish pigment instead. The inner limb is about as long but slightly broader than the outer, is longitudinally striated at its outer and granular at its inner part. It stains with hæmatoxylin, but not with osmic acid. Each rod is connected internally with a *rod fibre*, very fine, but here and there varicose; in the middle of the fibre is a *rod granule*, really the nucleus of the rod, striped broadly transversely, and situated about the middle of the external nuclear layer; the internal end of the rod fibre terminates in branchings in the outer molecular layer.

Each cone (fig. 573), like the rods, is made up of two limbs, outer and inner. The outer limb is tapering and not cylindrical like the corresponding part of the rod, and about one-third only of its length. There is, moreover, no visual purple found in the cones. The inner limb of the cone is broader in the centre. It is protoplasmic, and under the influence of light has been seen to execute movements. In birds, reptiles and amphibia, there is often a coloured oil globule present here. Each cone is in connection by its internal end with a *cone fibre*, which has much the same structure as the rod fibre, but is much stouter and has its nucleus (*cone granule*) quite near to the external limiting membrane. Its inner end terminates by branchings in the external molecular layer.

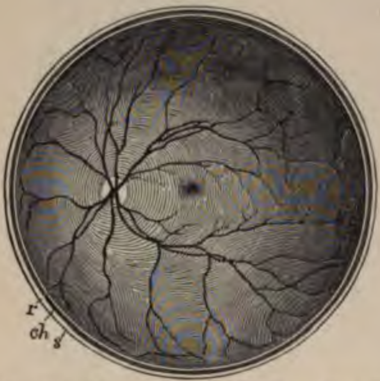

FIG. 574.—The posterior half of the retina of the left eye, viewed from before; *s*, the cut edge of the sclerotic coat; *ch*, the choroid; *r*, the retina; in the interior at the middle the macula lutea with the depression of the fovea centralis is represented by a slight oval shade; towards the left side the light spot indicates the colliculus or eminence at the entrance of the optic nerve, from the centre of which the arteria centralis is seen spreading its branches into the retina, leaving the part occupied by the macula comparatively free. (After Henle.)

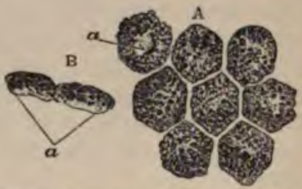

FIG. 575.—Pigment-cells from the retina. A, Cells still cohering, seen on their surface; *a*, nucleus indistinctly seen. In the other cells the nucleus is concealed by the pigment granules. B, Two cells seen in profile; *a*, the outer or posterior part containing scarcely any pigment. × 370. (Henle.)

In the rod and cone layer of birds, the cones usually predominate largely in number, whereas in man the rods are by far the more numerous, except in the fovea centralis, where cones only are present. The number of cones has been estimated at 3,000,000.

10. *Pigment-cell layer* consists of a single layer of polygonal cells, mostly six-sided, which send down a beard-like fringe to surround the outer ends of the rods. It is this layer which is continuous

with the uvea, where, however, the cells become rounded, and arranged two or three deep.

Differences in Structure of different parts.—Towards the centre of the *macula lutea* all the layers of the retina become greatly thinned out and almost disappear, except the rod and cone layer, and at the *fovea centralis* the rods disappear, and the cones are long and narrow. At the margin of the fovea the layers increase in thickness, and in the rest of the macula lutea are thicker than elsewhere. The ganglionic layer is especially thickened, the cells being six to eight deep (2, fig. 576). The bipolar inner granules (cone nuclei) are obliquely disposed (figs. 576 and 577) on the course of the cone fibres, and are situated at some distance from the *membrana limitans externa,* which is cupped towards the fovea (fig. 576). The yellow tint of the macula is due to a diffuse colouring matter in the interstices of the four or five inner layers; it is absent at the centre of the fovea.

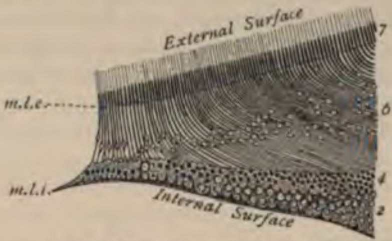

FIG. 576.—Diagram of a section through half the fovea centralis. 2, Ganglionic layer; 4, inner nuclear; 6, outer nuclear layer, the cone fibres forming the so-called *external fibrous layer;* 7, cones; *m.l.e.*, membrana limitans externa; *m.l.i.*, membrana limitans interna. (Schäfer and Golding Bird.)

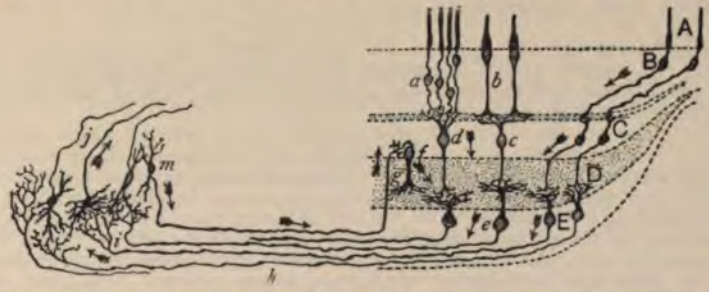

FIG. 577.—Scheme of the retinal elements. A, Cones of the fovea centralis; B, granules (nuclei) of these cones; C, synapse between the cones and bipolar cells in external molecular layer; D, synapse between the bipolar and ganglion cells in the internal molecular layer; *a* and *b*, rods and cones in other regions of the retina; *c*, bipolar cell destined for the cones; *d*, bipolar cell destined for the rods; E, *e*, ganglion cells; *f*, spongioblast; *g*, efferent fibre (? trophic), originating from the cell *m*, in geniculate body; *h*, optic nerve; *i*, terminal arborisations of optic nerve-fibres in geniculate body; *j*, fibres from the cells of geniculate body on the way to cerebral cortex. (R. y Cajal.)

It is important to notice what is clearly brought out in fig. 577, that at the fovea, each cone is connected to a separate chain of neurons, whereas in other regions the rods and cones are connected in groups to these chains; this explains the greater sensitiveness of foveal vision.

At the *ora serrata* the layers are not perfect, and disappear in this order: nerve-fibres and ganglion cells, then the rods, leaving only the inner limbs of the cones, next these cease, then the outer molecular layer, the inner and outer nuclear layers coalescing, and finally the inner molecular layer also is unrepresented.

At the *pars-ciliaris retinæ*, the retina consists of a layer of columnar cells, which probably represent the Müllerian fibres. These cells externally are in contact with the pigment layer of the retina, which is continued over the ciliary processes and back of the iris. Nervous structures are absent.

At the exit of the optic nerve the only structures present are nerve-fibres.

The anterior chamber is the space behind the cornea and in front of the iris. It is filled with aqueous humour (dilute lymph).

The vitreous humour, which is a jelly-like connective tissue (see p. 48), is situated behind the *crystalline lens.* It is enclosed in a membrane called *membrana hyaloidea,* which in front is continuous with the capsule of the lens; round the edge of the lens the canal left is called the *Canal of Petit* (fig. 561, p. 765), the membrane itself being the *Zonule of Zinn.* The hyaloid membrane separates the vitreous from the retina.

Blood-vessels of the Eyeball.—The eye is very richly supplied with blood-vessels. In addition to the conjunctival vessels which are derived from the palpebral and lacrimal arteries, there are at least two other distinct sets of vessels supplying the tunics of the eyeball.

(1) These are the short and long *posterior* ciliary arteries which pierce the sclerotic in the posterior half of the eyeball, and the *anterior* ciliary which enter near the insertions of the recti. These vessels anastomose and form a rich choroidal plexus; they also supply the iris and ciliary processes, forming a highly vascular circle round the outer margin of the iris and adjoining portion of the sclerotic. The distinctness of these vessels from those of the conjunctiva is well seen in the difference between the bright red of blood-shot eyes (conjunctival congestion), and the pink zone surrounding the cornea which indicates deep-seated ciliary congestion.

(2) The *retinal vessels* (fig. 574) are derived from the *arteria centralis retinæ,* which enters the eyeball along the centre of the optic nerve. They ramify all over the retina, in its inner layers. They can be seen by ophthalmoscopic examination.

The Eye as an Optical Instrument.

In a photographic camera images of external objects are thrown upon a screen at the back of a box, the interior of which is painted black. In the eye, the camera is represented by the eyeball with its black pigment, the screen by the layer of rods and cones of the retina, and the lens by the refracting media. In the case of the camera, the screen is enabled to receive clear images of objects at different distances, by an apparatus for focussing. The corresponding contrivance in the eye is called *accommodation*.

The iris, which allows more or less light to pass into the eye, corresponds with the diaphragms used in the photographic apparatus.

The refractive media are the cornea, aqueous humour, crystalline lens, and vitreous humour. The most refraction or bending of the rays of light occurs where they pass from the air into the cornea; they are again bent slightly in passing through the lens. Alterations in the anterior curvature of the lens lead to accommodation.

We may first consider the refraction through a transparent spherical surface, separating two media of different density.

The rays of light which fall upon the surface exactly perpendicularly do not suffer refraction, but pass through, cutting the optic axis (O A, fig. 578), a line which passes exactly through the centre of the surface, at a certain point, the *nodal point* (fig. 578, N), or centre of curvature. Any rays which do not so strike the curved surface are refracted towards the optic axis. Rays which impinge upon the spherical surface parallel to the optic axis, will meet at a point behind, upon the said axis which is called the *chief posterior focus* (fig. 578, F_1); and again there is a point on the optic axis in front of the surface, rays of light from which so strike the surface that they are refracted in a line parallel with the axis $d\,f'$; this point (fig. 578, F_2) is called the *chief anterior focus*. The optic axis cuts the surface at what is called the *principal point*.

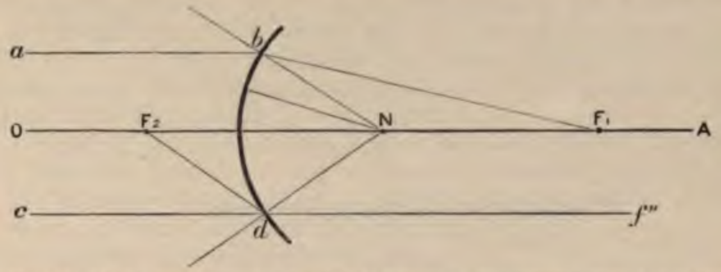

FIG. 578.—Diagram of a simple optical system (after M. Foster). The curved surface, *b*, *d*, is supposed to separate a less refractive medium towards the left from a more refractive medium towards the right.

It is quite obvious that the eye is a much more complicated optical apparatus than the one described in the figure. It is, however, possible to reduce the refractive surfaces and media to a simpler form when the refractive indices of the different media and the curvature of each surface are known. These data are as follows:—

Index of refraction of cornea . . . . = 1·37
" " aqueous and vitreous . = 1·34 to 1·36
" " lens . . . . . = 1·4 in outer to 1·45 in inner part.
Radius of curvature of cornea . . . . = 7·8 mm.
" " anterior surface of lens = 10 "
" " posterior . . . . = 6 "
Distance from anterior surface of cornea to anterior surface of lens . . . . . = 3·6 "
Distance from posterior surface of cornea to posterior surface of lens . . . . = 7·2 "
Distance from posterior surface of lens to retina . . . . = 15·0 "

With these data it has been found comparatively easy to reduce by calculation the different surfaces of different curvature into one mean curved surface of known curvature, and the differently refracting media into one mean medium the refractive power of which is known.

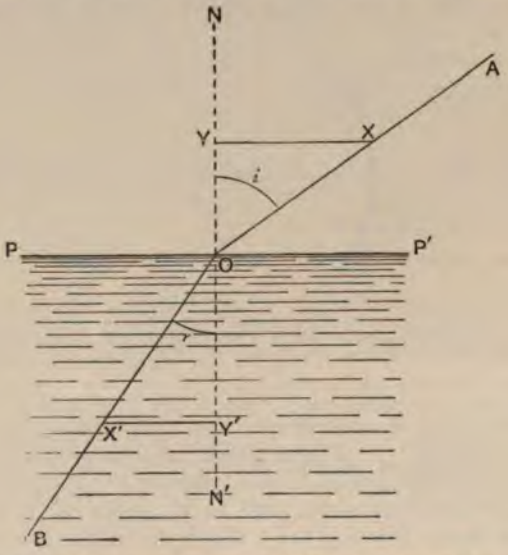

FIG. 579.—If P P′ is a line which separates two media, the lower one being the denser, and A O is a ray of light falling on it, it is bent at O towards the normal or perpendicular line N N′. A O is called the incident ray, and O B the refracted ray; A O N is called the angle of incidence (*i*), N′ O B the angle of refraction (*r*). If any distance O X is measured off along O A, and an equal distance O X′ along O B and perpendiculars drawn to N N′; then $\frac{XY}{X'Y'}$ = index of refraction.

The simplest so-called schematic eye formed upon this principle, suggested by Listing as *the reduced eye*, has the following dimensions:—

From anterior surface of cornea to the principal point = 2·3448 mm.
From the nodal point to the posterior surface of lens = ·4764 ,,
Posterior chief focus lies behind cornea . . . = 22·8237 ,,
Anterior chief focus in front of cornea . . . = 12·8326 ,,
Radius of curvature of ideal surface . . . . = 5·1248 ,,

The term index of refraction means the ratio of the sine of the angle of incidence to that of the angle of refraction; this is explained in the small text beneath fig. 579.

In this reduced or simplified eye, the principal posterior focus, about 23 mm. behind the spherical surface, would correspond to the position of the retina behind the anterior surface of the cornea. The refracting surface would be situated about midway between the posterior surface of the cornea and the anterior surface of the lens.

The *optical axis* of the eye is a line drawn through the centres of curvature of the cornea and lens, prolonged backwards to touch the retina between the porus opticus and fovea centralis, and this differs from the *visual axis* which passes through the nodal point of the reduced eye to the fovea centralis; this forms an angle of 5° with the optical axis. But for practical purposes the optical axis and the visual axis may be considered to be identical.

The *visual* or *optical angle* (fig. 580) is included between the lines drawn from the borders of any object to the nodal point; if the lines are prolonged backwards they include an equal angle. It has been shown by Helmholtz that the smallest angular distance between two points which can be appreciated as two distinct points = 50 seconds, the size of the retinal image being $3{\cdot}65\mu$; this is a little more than the diameter of a cone at the fovea centralis which = 3μ, the distance between the centres of two adjacent cones being = 4μ. If the two points are so close together that they subtend a visual angle less than 50 seconds, both images will fall upon one cone, and the two points will therefore appear as one.

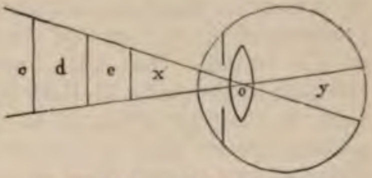

FIG. 580.—Diagram of the optical angle.

Any object, for example, the arrow A B (fig. 581), may be considered as a series of points from each of which a pencil of light diverges to the eye. Take, for instance, the rays diverging from the tip of the arrow A; C C represents the curvature of the schematic or reduced eye; the ray which passes through the centre of the circle of which C C is part is not refracted; this point is represented as an asterisk in fig. 581; it is near the posterior surface of the crystalline lens; the ray A C, which is parallel to the optic axis O O′, is refracted through the principal posterior focus P, and cuts the first ray at the point A′ on the retina. All the other rays from A meet at the same point. Similarly the other end of the arrow B is focussed at B′, and rays from all other points have corresponding focusses.

It will thus be seen that an inverted image of external objects is formed on the retina. The retina is a curved screen, but the images fall only on a small area of the retina under normal circumstances; hence, for practical purposes, this small area may be regarded as flat.

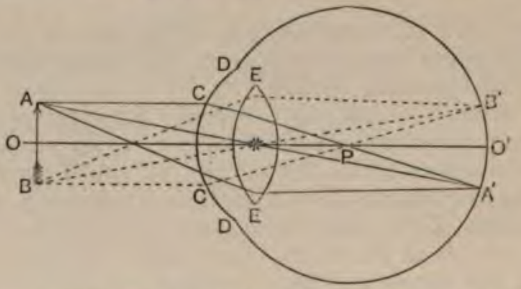

FIG. 581.—Diagram of the course of the rays of light, to show how an image is formed upon the retina. The surface C C should be supposed to represent the ideal curvature.

The question then arises, Why is it that objects do not appear to us to be upside down? This is easily understood when we remember that the *sensation* of sight occurs not in the eye, but in the brain. By education the brain learns that the tops of objects excite certain portions of the retina, and the lower parts of objects other portions of the retina. That these portions of the retina are reversed in position to the parts of the object does not matter at all, any more than it matters when one's photograph arrives home from the photographer's that it was wrong way up in the photographer's camera—one puts it right way up in the photograph album.

ACCOMMODATION

The power of accommodation is primarily due to an ability to vary the shape of the lens; its front surface becomes more or less convex, according as the distance of the object looked at is near or far. The nearer the object, the more convex, up to a certain limit, the front surface of the lens becomes, and *vice versâ;* the back surface takes no share in the production of the effect required. The posterior surface, which during rest is more convex than the anterior, is thus rendered the less convex of the two during accommodation. The following simple experiment illustrates this point: If a lighted candle be held a little to one side of a person's eye an observer looking at the eye from the other side sees three images of the flame (fig. 582). The first and brightest is (1) a small erect image formed by the anterior convex surface of the cornea; the second (2) is also erect, but larger and less distinct than the preceding, and is formed at the anterior convex surface of the lens; the third (3) is smaller, inverted, and indistinct; it is formed at the posterior surface of the lens, which is concave forwards, and therefore, like all concave mirrors, gives an inverted image. If now the eye under observation is made to look at a near object, the second image becomes smaller, clearer, and approaches the first. If the eye is now adjusted for a far point, the second image enlarges again, becomes less distinct, and recedes from the first. In both cases the first and third images remain unaltered in size, distinctness, and position. This proves that during accommodation for near objects the curvature of the cornea, and of the *posterior surface* of the lens, remain unaltered, while the *anterior* surface of the lens becomes more convex and approaches the cornea.

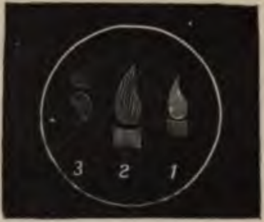

FIG. 582.—Diagram showing three reflections of a candle. 1, From the anterior surface of cornea; 2, from the anterior surface of lens; 3, from the posterior surface of lens.

The experiment is more striking when two bright images (represented by arrows in fig. 583) are used; the two images from the front surface of the lens during accommodation not only approach those from the cornea, but also approach one another, and become somewhat smaller. (*Sanson's Images*). Helmholtz's Phakoscope (fig. 584) is a triangular box with arrangements for demonstrating this experiment.

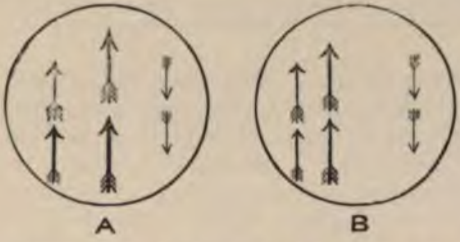

FIG. 583.—Diagram of Sanson's images. A, When the eyes are not, and B, when they are focussed for near objects. The fig. to the right in A and B is the inverted image from the posterior surface of the lens.

Mechanism of Accommodation.—The lens having no inherent power of contraction, its changes of outline must be produced by some power from without; this power is supplied by the ciliary muscle. Its action is to draw forwards the choroid, and by so doing to slacken the tension of the suspensory ligament of the lens which arises from it. The anterior surface of the lens is kept flattened by the action of this ligament. The ciliary muscle during accommodation, by diminishing its tension, diminishes to a proportional degree the flattening of which it is the cause. On diminution or cessation of the action of the ciliary muscle, the lens returns to its former shape, by virtue of the elasticity of the suspensory ligament (fig. 585). From this it will appear that the eye is usually focussed for distant objects. In viewing near objects the ciliary muscle contracts; the ciliary muscle relaxes on withdrawal of the attention from near to distant objects.

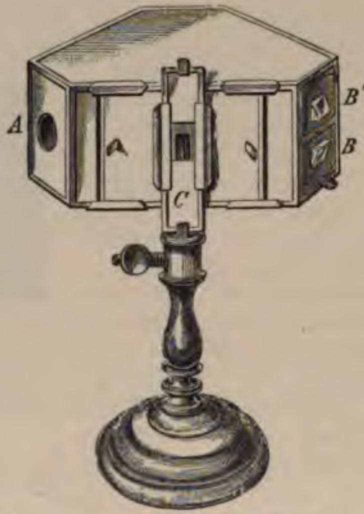

FIG. 584.—Phakoscope of Helmholtz. At *B B'* are two prisms, by which the light of a candle is concentrated on the eye of the person experimented with, which is looking through a hole in the third angle of the box opposite to the window *C*. *A* is the aperture for the eye of the observer. The observer notices three double images, represented by arrows, in fig. 583, reflected from the eye under examination when the eye is fixed upon a distant object; the position of the images having been noticed, the eye is made to focus a near object, such as a reed pushed up at *C*; the images from the anterior surface of the lens will be observed to move as described in the text.

It is possible to calculate the curvature of the lens or cornea in the body, by measuring the size of the image of an object upon it. The radius (r) of curvature of a convex reflecting surface is given by the formula $r = \frac{2ab}{c}$; a is the distance of the object from the surface, b the diameter of the image, and c that of the object. a and c are easily measured; b is measured by Helmholtz's *ophthalmometer*, the principle of which is as follows:—If a line is looked at through a plate of glass placed obliquely between it and the eye, the line is shifted sideways to either right or left; if the glass plate is then placed obliquely at right angles to its previous position, the line is shifted in the opposite direction. In the ophthalmometer there are two glass plates intersecting each other at an angle; the image of a bright horizontal line upon the lens or cornea is looked at through the junction between the two plates; one plate shifts the image to the right, the other to the left; the angle between the two plates is altered until the line appears as two distinct lines just touching each other. The amount of shifting of each, which must therefore be half the length of the image of the line, can be easily calculated if the thickness of the glass plates, their refractive index, and the angle between them are known. Double this result gives the size of the image on the surface under investigation.

Range of Distinct Vision. Near-point.—In every eye there is a limit to the power of accommodation. If a book be brought nearer and nearer to the eye, the type at last becomes indistinct, and cannot be brought into focus by any effort of accommodation, however strong. This, which is termed the *near-point*, can be determined by the following experiment (*Scheiner*). Two small holes are pricked in a card with a pin not more than a twelfth of an inch (2 mm.) apart; at any rate their distance from each other must not exceed the diameter of the pupil. The card is held close in front of the eye, and a small needle viewed through the pin-holes. At a moderate distance it can be clearly focussed, but when brought nearer, beyond a certain point, the image appears double, or at any rate blurred. This point where the needle ceases to appear single is the near-point. Its distance from the eye can of course be readily measured. It is usually about 5 or 6 inches (13 cm.). In the accompanying figure (fig. 586) the lens *b* represents the refractive apparatus of the eye; *e* and *f* the two pin-holes in the card, *nn* the retina; *a* represents the position of the needle. When the needle is at a moderate distance, the two pencils of light coming from *e* and *f* are focussed at a single point on the retina *nn*. If the needle is brought nearer than the near-point, the strongest effort of accommodation is not sufficient to

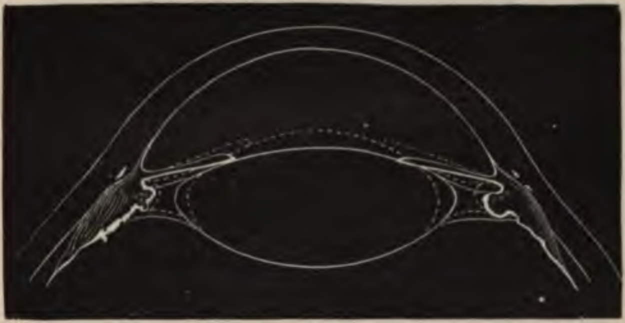

FIG. 585.—Diagram representing by dotted lines the alteration in the shape of the lens on accommodation for near objects. (E. Landolt.)

focus the two pencils, they meet at a point behind the retina. The effect is the same as if the retina were shifted forward to *mm*. Two images *h.g.* are formed, one from each hole. It is interesting to note that when two images are produced, the lower one *g* really appears in the position Q, while the upper one appears in the position P. This may be readily verified by covering the holes in succession.

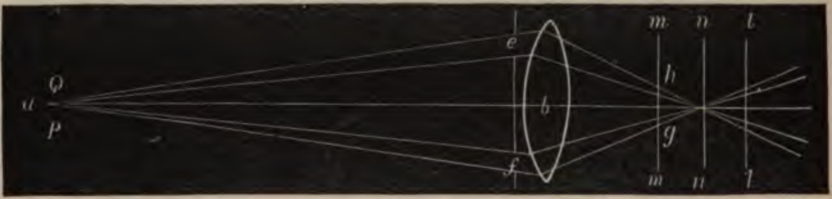

FIG. 586.—Diagram of experiment to ascertain the minimum distance of distinct vision.

During accommodation two other changes take place in the eyes: (1) *The eyes converge* owing to the action of the internal rectus muscle of each eyeball. (2) *The pupils contract.*

The contraction of all of the muscles which have to do with accommodation, viz., of the ciliary muscle, of the internal recti muscles, and of the sphincter pupillæ, is under the control of the third nerve. It should further be noted that although the act is a voluntary one, the fibres of the ciliary muscle and of the sphincter pupillæ are of the plain variety.

The account of accommodation as given in the preceding pages is true for man and other mammals, birds, and certain reptiles.

Beer has, however, shown that in many animals lower in the scale, the mechanism of accommodation varies a good deal, and is often very different from that just described, consisting, in fact, in a power of altering the distance between the lens and the retina.

In bony fishes, the eye at rest is accommodated for near objects; in focussing for distant objects the lens is drawn nearer to the retina by a special muscle called the *retractor lentis*. In cephalopods the same occurs, but the retractor lentis is absent; here the approach of the lens to the retina is brought about by an alteration of intra-ocular tension. In Amphibia and most snakes, the eye at rest is focussed for distant objects; in accommodating for near objects the lens, by alteration of intra-ocular tension, is brought forward, that is, the distance between it and the retina is increased. There appear to be not a few animals in all classes which do not possess the power of accommodation at all. Indeed, Barrett states this is so for most mammals.

DEFECTS IN THE OPTICAL APPARATUS

Under this head we may consider the defects known as (1) Myopia, (2) Hypermetropia, (3) Astigmatism, (4) Spherical Aberration, (5) Chromatic Aberration.

The normal (*emmetropic*) eye is so adjusted that at rest parallel rays are brought exactly to a focus on the retina (1, fig. 587). Hence all objects except near ones (practically all objects more than twenty feet off) are seen without any effort of accommodation; in other words, the far-point of the normal eye is at an infinite distance.

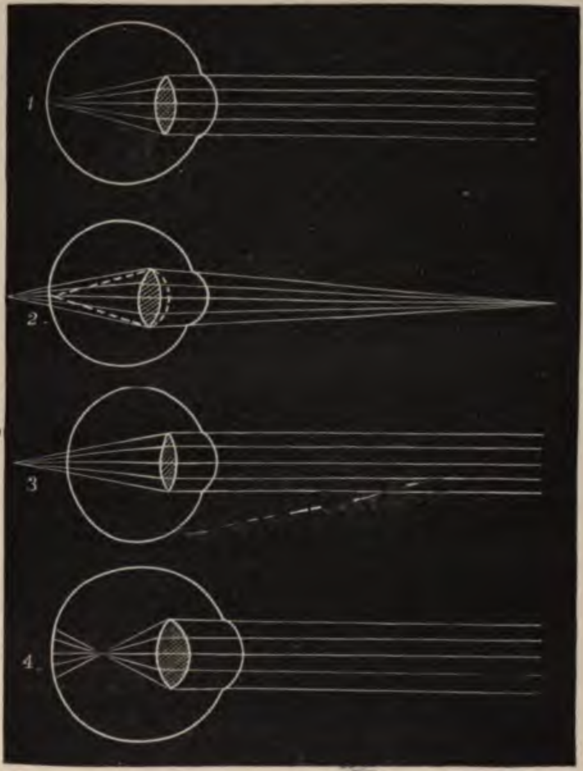

FIG. 587.—Diagram showing—1, normal (*emmetropic*) eye bringing parallel rays exactly to a focus on the retina; 2, normal eye adapted to a near-point; without accommodation the rays would be focussed behind the retina, but by increasing the curvature of the anterior surface of the lens (shown by a dotted line) the rays are focussed on the retina (as indicated by the meeting of the two dotted lines); 3, *hypermetropic* eye; in this case the axis of the eye is shorter than normal; parallel rays are focussed behind the retina; 4, *myopic* eye; in this case the axis of the eye is abnormally long; parallel rays are focussed in front of the retina. The figure incorrectly represents the refraction as occurring only in the crystalline lens; the principal refraction really occurs at the anterior surface of the cornea.

In viewing near objects we are conscious of the effort (the contraction of the ciliary muscle) by which the anterior surface of the lens is rendered more convex, and rays which would otherwise be focussed *behind* the retina are converged upon the retina (see dotted lines, 2, fig. 587).

1. *Myopia* (short-sight), (4, fig. 587).—This defect is due to an

abnormal elongation of the eyeball. The retina is too far from the lens, and consequently parallel rays are focussed *in front of* the retina, and, crossing, form little circles on the retina; thus the images of distant objects are blurred and indistinct. The eye is, as it were, permanently adjusted for a near-point. Rays from a point near the eye are exactly focussed on the retina. But those which issue from any object beyond a certain distance (*far-point*) cannot be distinctly focussed. This defect is corrected by *concave* glasses which cause the rays entering the eye to diverge: hence they do not come to a focus so soon. Such glasses, of course, are only needed to give a clear vision of distant objects. For near objects, except in extreme cases, they are not required.

2. *Hypermetropia* (3, fig. 587).—This is the reverse defect. The eyeball is too short. Parallel rays are focussed *behind* the retina: an effort of accommodation is required to focus even parallel rays on the retina; and when they are divergent, as in viewing a near object, the accommodation is insufficient to focus them. Thus, in well-marked cases, distant objects require an effort of accommodation, and near ones a very powerful effort, and the ciliary muscle is, therefore, constantly acting. This defect is obviated by the use of *convex* glasses, which render the pencils of light more convergent. Such glasses are, of course, especially needed for near objects, as in reading, etc. They rest the eye by relieving the ciliary muscle from excessive work.

3. *Astigmatism.*—This defect, which was first discovered by Airy, is due to a greater curvature of the eye in one meridian than in others. The eye may be even myopic in one plane, and hypermetropic in others. Thus vertical and horizontal lines crossing each other cannot both be focussed at once; one set stand out clearly, and the others are blurred and indistinct. This defect, which is present in a slight degree in all eyes, is generally seated in the cornea, but occasionally in the lens as well; it may be corrected by the use of cylindrical glasses (*i.e.*, curved only in one direction).

4. *Spherical Aberration.*—The rays of a cone of light from an object situated at the side of the field of vision do not meet all in the same point, owing to their unequal refraction; for the refraction of the rays which pass through the circumference of a lens is greater than that of those traversing its central portion. This defect is known as *spherical aberration*, and in the camera, telescope, microscope, and other optical instruments, it is remedied by the interposition of a screen with a circular aperture in the path of the rays of light, cutting off all the marginal rays, and only allowing the passage of those near the centre. Such correction is effected in the eye by the iris, which prevents the rays from passing through any part of the refractive apparatus but its centre. The image of an

object will be most defined and distinct when the pupil is narrow, the object at the proper distance for vision, and the light abundant; so that, while a sufficient number of rays are admitted, the narrowness of the pupil may prevent the production of indistinctness of the image by *spherical aberration.*

Distinctness of vision is further secured by the pigment of the outer surface of the retina, the posterior surface of the iris and the ciliary processes, which absorbs most of the light which is reflected within the eye, and prevents its being thrown again upon the retina so as to interfere with the images there formed.

5. *Chromatic Aberration.*—In the passage of light through an ordinary convex lens, decomposition of each ray into its elementary colours commonly ensues, and a coloured margin appears around the image, owing to the unequal refraction which the elementary colours undergo. In optical instruments this, which is termed *chromatic aberration,* is corrected by the use of two or more lenses, differing in shape and density, the second of which continues or increases the refraction of the rays produced by the first, but by recombining the individual parts of each ray into its original white light, corrects any chromatic aberration which may have resulted from the first. It is probable that the unequal refractive power of the transparent media in front of the retina may be the means by which the eye is enabled to guard against the effect of chromatic aberration. The human eye is achromatic, however, only so long as the image is received at its focal distance upon the retina, or so long as the eye is properly accommodated. If these conditions are interfered with, a more or less distinct appearance of colours is produced.

From the insufficient adjustment of the image of a small white object, it appears surrounded by a sort of halo or fringe. This phenomenon is termed *Irradiation.* It is partly [*] for this reason that a white square on a black ground appears larger than a black square of the same size on a white ground. The phenomenon is naturally more marked when the white object is a little out of focus.

Defective Accommodation—Presbyopia.—This condition is due to the gradual loss of the power of accommodation which is an early sign of advancing years. In consequence, the person is obliged in reading to hold the book further and further away in order to focus the letters, till at last the letters are held too far for distinct vision. The defect is remedied by weak convex glasses. It is due chiefly to the gradual increase in density of the lens, which is unable to swell out and become convex when near objects are looked at, and also to a weakening of the ciliary muscle, and a general loss of elasticity in the parts concerned in the mechanism.

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[*] The phenomenon is also partly due to what is called "spatial induction."

FUNCTIONS OF THE IRIS.

The iris has three uses:—

1. To act as a diaphragm in order to lessen spherical aberration in the manner just described.

2. To regulate the amount of light entering the eye. In a bright light the pupil contracts; in a dim light it enlarges. This may be perfectly well seen in one's own iris by looking at it in a mirror while one alternately turns a gas-light up and down.

3. By its contraction during accommodation it supports the action of the ciliary muscle.

The muscular fibres (unstriped in mammals, striped in birds) of the iris are arranged circularly around the margin of the pupil, and radiatingly from its margin. The radiating fibres are best seen in the eyes of birds and otters; some look upon them as elastic in nature, but there is little doubt that they are contractile. Those who believe they are not contractile explain dilatation of the pupil as due to inhibition of the circular fibres. But if the iris is stimulated near its outer margin at three different points simultaneously the pupil assumes a triangular shape, the angles of the triangle corresponding to the points stimulated; this must be due to contraction of three strands of the radiating muscle; inhibition of the circular fibres would occur equally all round.

The iris is supplied by three sets of nerve-fibres contained in the ciliary nerves.

(*a*) The third nerve *viâ* the short ciliary nerves supplies the circular fibres.

(*b*) The cervical sympathetic supplies the radiating fibres. The cilio-spinal centre which governs them is in the cervical region of the cord (see p. 676). The fibres leave the cord by the anterior root of the second thoracic nerve, pass into the cervical sympathetic, and reach the eyeball *viâ* the ophthalmic branch of the fifth, and long ciliary nerves.

(*c*) Fibres of the fifth nerve which are sensory.

The experiments on these nerves are those of section and stimulation of the peripheral ends; the usual experiments by which the functions of a motor nerve are discovered.

Nerve.	Experiment.	Effect on pupil.
Third . . .	Section . .	Dilatation.
Third . . .	Stimulation .	Contraction.
Sympathetic . .	Section . .	Contraction.
Sympathetic . .	Stimulation .	Dilatation.
Both nerves together	Stimulation	Contraction overcomes the dilatation.

Certain drugs dilate the pupil. These are called *mydriatics;* atropine is a well-known example. Others cause the pupil to contract. These are called *myotics;* physostigmine and opium (taken internally) are instances. Different myotics and mydriatics act in different ways, some exerting their activity on the muscular, and others on the nervous structures of the iris.

Reflex actions of the iris.—When the iris contracts under the influence of light, the sensory nerve is the optic, and the motor the third nerve. The central connection of the two nerves in the region of the mid-brain we shall see later on. The iris also contracts on accommodation; and the reflex path concerned in this action is a different one from that concerned in the light reflex, as this reflex often remains in cases of locomotor ataxy, after there is an entire loss of the reflex to light (Argyll-Robertson pupil).

On painful stimulation of any part of the body, there is reflex dilatation of the pupil. This is accompanied by starting of the eyeballs, due to contraction of the plain muscle in the capsule of Tenon, which, like the dilator fibres of the iris, is supplied by the cervical sympathetic nerve.

We may sum up the principal conditions under which the pupil contracts and dilates in the following table:—

Causes of—

Contraction of the Pupil.	**Dilatation of the Pupil.**
1. Stimulation of third nerve.	1. Paralysis of the third nerve.
2. Paralysis of cervical sympathetic.	2. Stimulation of the cervical sympathetic.
3. When the eye is exposed to light.	3. In the dark.
4. When accommodation occurs.	4. When the accommodation is relaxed.
5. Under the local influence of physostigmine.	5. Under the local influence of atropine. This drug also paralyses the ciliary muscle.
6. Under the influence of opium.	6. In the last stage of asphyxia.
7. During sleep.	7. In deep chloroform narcosis.
	8. Under the influence of certain emotions, such as fear.
	9. During pain.

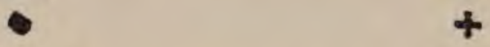
There is a close connection of the centres that govern the activity of the two irides. If one eye is shaded by the hand, its pupil will of course dilate, but the pupil of the other eye will also dilate. The two pupils always contract or dilate together unless the cause is the local injury to the nerves of one side or the local action of drugs.

FUNCTIONS OF THE RETINA.

The Retina is the nervous coat of the eye; it contains the layer of nerve-epithelium (rods and cones) which is capable of receiving the stimulus of light, and transforming it into a nervous impulse which passes to the brain by the optic nerve.

The bacillary layer, or layer of rods and cones, is at the back of all the other retinal layers, which the light has to penetrate before it can affect this layer. The proofs of the statement that it is the layer of the retina which is capable of stimulation by light are the following:—

(1) The point of entrance of the optic nerve into the retina, where the rods and cones are absent, is insensitive to light, and is called the *blind spot.* This is readily demonstrated by what is known as Mariotte's experiment. If we direct one eye, the other being closed, upon a point at such a distance to the side of any object, that the image of the latter must fall upon the retina at the point of entrance of the optic nerve, this image is lost. If, for example, we close the left eye, and look steadily with the right eye at the dot here represented, while the page is held about six inches from the eye, both dot and cross are visible. On gradually increasing the distance between the page and the eye, still keeping the right eye steadily on the dot, it will be found that suddenly the cross disappears from view, because its image has fallen on the blind spot; on removing the book still farther, it comes in sight again. The question has arisen why we are not normally conscious of a gap in the image. The gap is not felt for the reason that a defect of light sensations at a spot blind from the beginning can no more be perceived as a gap in the image than the blindness, say, of the skin of the back or foot can be so perceived.



(2) In the fovea centralis which contains rods and cones but no optic nerve-fibres, and in which the other layers of the retina are thinned down to a minimum, light produces the greatest effect. In the macula lutea, cones occur in large numbers, and in the fovea centralis cones without rods are found, whereas, in the rest of the retina which is not so sensitive to light, there are fewer cones than rods.

(3) If a small lighted candle is moved to and fro at the side of and close to one eye in a darkened room, while the eyes look steadily forward on to a dull background, a remarkable branching figure (*Purkinje's figures*) is seen floating before the eye, consisting of dark lines on a reddish ground. As the candle moves, the figure moves in the opposite direction, and from its whole appearance there can be no doubt that it is a reversed picture of the retinal vessels pro-

jected before the eye.* This remarkable appearance is due to shadows of the retinal vessels cast by the candle; and it is only when they are thrown upon the retina in an unusual slanting direction that they are perceived. The branches of these vessels are distributed in the nerve-fibre and ganglionic layers; and since the light of the candle falls on the retinal vessels from in front, the shadow is cast behind them, and hence those elements of the retina which perceive the shadows must also lie behind the vessels. Here, then, we have a clear proof that the light-perceiving elements are not the inner, but one of the external layers of the retina; further than this, calculation has shown it is the layer of rods and cones. The data for such a calculation are—the dimensions of the eyeball, the distance of the screen from the eye, the angle through which the candle is moved, and the displacement of the figure seen.

Duration of Visual Sensations.—The duration of the sensation produced by a luminous impression on the retina is always greater than that of the impression which produces it. However brief the luminous impression, the effect on the retina always lasts for about one-eighth of a second. Thus, supposing an object in motion, say a horse, to be revealed on a dark night by a flash of lightning. The object would be seen apparently for an eighth of a second, but it would not appear in motion; because, although the image remained on the retina for this time, it was really revealed for such an extremely short period (a flash of lightning lasting only a millionth of a second) that no appreciable movement on the part of the object could have taken place in the period during which it was revealed to the retina of the observer. The same fact is proved in a reverse way. The spokes of a rapidly revolving wheel are not seen as distinct objects, because at every point of the field of vision over which the revolving spokes pass, a given impression has not faded before another replaces it. Thus every part of the interior of the wheel appears occupied.

The stimuli which excite the retina are exceedingly slight; for instance, the minimum stimulus in the form of green light is equal in terms of work to that which is done in raising a ten-millionth part of a milligramme to the height of a millimetre, and even some of this is doubtless wasted in the form of heat. The time during which the stimulus acts may be excessively small, thus light from a rapidly rotating mirror is visible even when it only falls upon the retina for one eight-millionth part of a second. Some physiologists have drawn an analogy between retinal and muscular excitations. There is no complete analogy, but the following points of resemblance may be noted:—

1. The retina like the muscle possesses a store of potential energy, which the stimulus serves to fire off.
2. Fatigue on action, and recovery after rest are noticeable in both.

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* Purkinje's figures can be much more readily seen by simply looking steadily down a microscope, and moving the whole instrument backwards and forwards, or from side to side, while so doing.

3. The curve of retinal excitation, like the muscle curve, rises not abruptly but gradually to its full height, and on the cessation of the stimulus takes a measurable time to fall again, the retinal impression outlasting the stimulus by about one-eighth of a second.

4. With comparatively slow intermittent excitation, the phenomenon known as *flicker* takes place; this may be shown by the slow rotation on Maxwell's machine of a disc painted with alternate black and white sectors. This roughly corresponds with what in a muscle is called incomplete tetanus.

5. When the rate of stimulation is increased, as by increasing the speed of rotation of the disc just alluded to (say to twenty or thirty times a second) the resulting sensation is a smooth one of greyness. This fusion of individual stimuli into a continuous sensation, does not by any means correspond to the complete tetanus of muscle, for the resultant sensation has a brightness corresponding not to a summation of the individual fusing sensations, but to a brightness which would ensue if the stimuli were spread evenly over the surface of the disc (Talbot's Law).

The Ophthalmoscope.

Every one is perfectly familiar with the fact, that it is quite impossible to see the *fundus* or back of another person's eye by simply looking into it. The interior of the eye forms a perfectly black background.* The same remark applies to the difficulty we experience in seeing into a room from the street through the window unless the room is lighted within. In the case of the eye this fact is partly due to the feebleness of the light reflected from the retina, most of it being absorbed by the retinal pigment; but far more to the fact that every such ray is reflected straight to the source of light (*e.g.*, candle), and cannot, therefore, be seen by the unaided eye without intercepting the incident light from the candle, as well as the reflected rays from the retina. This difficulty is surmounted by the use of the *ophthalmoscope.*

The ophthalmoscope was invented by Helmholtz; as a mirror for reflecting the light into the eye, he employed a bundle of thin glass plates; this mirror was transparent, and so he was able to look through it in the same direction as that of the rays of the light it reflected. It is almost impossible to over-estimate the boon this instrument has been to mankind; previous to this in the examination of cases of eye disease, the principal evidence on which the surgeon had to rely was that derived from the patient's sensations; now he can look for himself.

The instrument, however, has been greatly modified since Helmholtz's time; the principal modification is the substitution of a concave mirror of silvered glass for the bundle of glass plates; this is mounted on a handle, and is perforated in the centre by a small hole through which the observer can look.

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* In some animals (*e.g.*, the cat), the pigment is absent from a portion of the retinal epithelium; this forms the *Tapetum lucidum.* The use of this is supposed to be to increase the sensitiveness of the retina, the light being reflected back through the layer of rods and cones. It is certainly the case that these animals are able to see clearly with less light than we can, hence the popular idea that a cat can see in the dark. In fishes a tapetum lucidum is often present; here the brightness is increased by crystals of guanine.

The methods of examining the eye with this instrument are—the *direct* and the *indirect:* both methods of investigation should be employed. A drop of a solution of atropine (two grains to the ounce) or of homatropine hydrobromate, should be instilled about twenty minutes before the examination is commenced; the ciliary muscle is thereby paralysed, the power of accommodation is abolished, and the pupil is dilated. This will materially facilitate the examination; but it is quite possible to observe all the details to be presently described without the use of such drugs. The room being now darkened, the observer seats himself in front of the person whose eye he is about to examine, placing himself upon a somewhat higher level. Let us suppose that the right eye of the patient is being examined. A brilliant and steady light is placed close to the left ear of the patient. Taking the mirror in his right hand, and looking through the central hole, the operator directs a beam of light into the eye of the patient. A red glare, known as *the reflex*, is seen; it is due to the illumination of the retina. The patient is then told to look at the little finger of the observer's right hand as he holds the mirror; to effect this the eye is rotated somewhat inwards, and at the same time the reflex changes from red to a lighter colour, owing to the reflection from the optic disc. The observer now approximates the mirror, with his eye to the eye of the patient, taking care to keep the light fixed upon the pupil, so as not to lose the reflex. At a certain point, which varies with different eyes, but is usually reached when there is an interval of about two or three inches between the observed and the observing eye, *the vessels of the retina* become visible. Examine carefully the fundus of the eye, *i.e.*, the red surface—until *the optic disc* is seen; trace its circular outline, and observe the small central white spot, the porus opticus, or *physiological pit:* near the centre is the central artery of the retina breaking up upon the disc into branches; veins also are present, and correspond roughly to the course of the arteries. Trace the vessels over the disc on to the retina. Somewhat to the outer side, and only visible after some practice, is the *yellow spot*, with the smaller lighter-coloured *fovea centralis* in its centre. This constitutes the direct method of examination; by it the various details of the fundus are seen as they really exist, and it is this method which should be adopted for ordinary use.

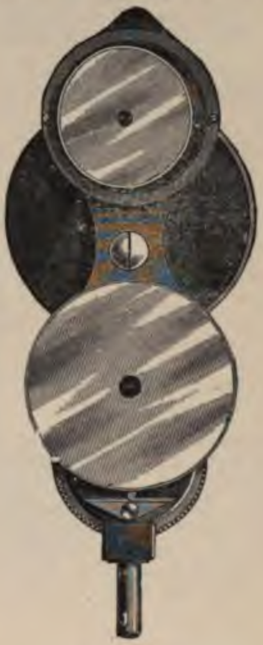

FIG. 588.—The Ophthalmoscope. The small upper mirror is for direct, the larger for indirect, illumination.

If the observer is myopic or hypermetropic, he will be unable to employ the direct method of examination until he has remedied his defective vision by the use of proper glasses.

In the indirect method the patient is placed as before, and the operator holds the mirror in his right hand at a distance of twelve to eighteen inches from the patient's right eye. At the same time he rests his left little finger lightly upon the patient's right temple, and holding a convex lens between his thumb and forefinger, two or three inches in front of the patient's eye, directs the light through the lens into the eye. The red reflex, and subsequently the white one, having been gained, the operator slowly moves his mirror, and with it his eye, towards or away from the face of the patient, until the outline of one of the retinal vessels becomes visible, when very slight movements on the part of the operator will suffice to bring into view the details of the fundus above described, but the image will be much smaller and inverted. The appearances seen are depicted in fig. 574. The lens should be kept fixed at a distance of two or three inches, the mirror alone being moved until the disc becomes visible: should the image of the mirror, however, obscure the disc, the lens may be slightly tilted.

The two next figures show diagrammatically the course of the rays of light.

Fig. 589 represents what occurs when employing the direct method. S is the

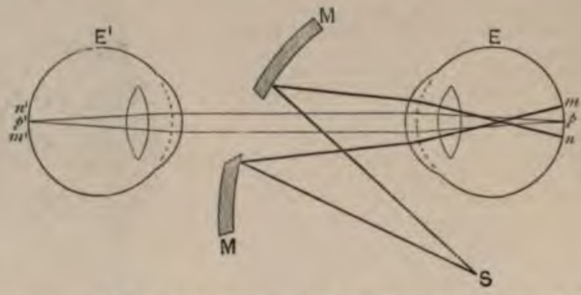

FIG. 589.—The course of the light in examining the eye by the direct method. (T. G. Brodie.)

source of light, and M M the concave mirror with its central aperture, which reflects the rays; these are focussed by the eye E, which is being examined, to a point in the vitreous humour, and this produces a diffuse lighting of the interior of the eyeball. Rays of light issuing from the point p emerge from the eye parallel to one another, and enter the observer's eye E^1; they are brought to a focus p^1 on the retina as the eye is accommodated for distant vision. Similarly the point m and n will give rise to images at m^1 and n^1 respectively.

Fig. 590 represents what occurs in examining the eye by the indirect method.

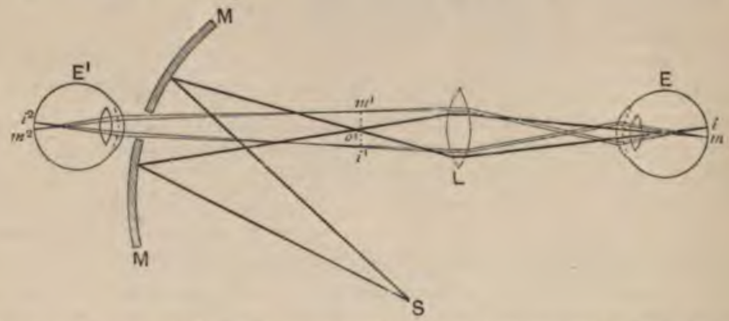

FIG. 590.—The course of the light in examining the eye by the indirect method. (T. G. Brodie.)

S is the source of light, M M the mirror, E the observed, and E^1 the observing eye as before. The rays of light are reflected from the mirror and form an image at o^1; they then diverge and are again made convergent by the lens L held in front of the eye by the observer; by this means a second image is focussed just behind the crystalline lens of the eye E. They then again diverge and diffusely light up the interior of the eyeball. The rays of light reflected from two points i and m on the retina diverging from the eye are refracted to the glass lens L, and give an inverted real image i^1 m^1 larger than the object i m. These latter rays then diverge, and are collected and focussed by the observing eye E^1 to give an image i^2 m^2 on the retina. (T. G. Brodie.)

The Perimeter.

This is an instrument for mapping out the field of vision. It consists of a graduated arc, which can be moved into any position, and which when rotated traces out a hollow hemisphere. In the centre of this the eye under examination is placed, the other eye being closed. The examiner then determines on the surface of the hemisphere those points at which the patient just ceases or just begins to see a small object moved along the arc of the circle. These points are plotted out on a chart graduated in degrees, and by connecting them the outline of the field of vision is obtained.

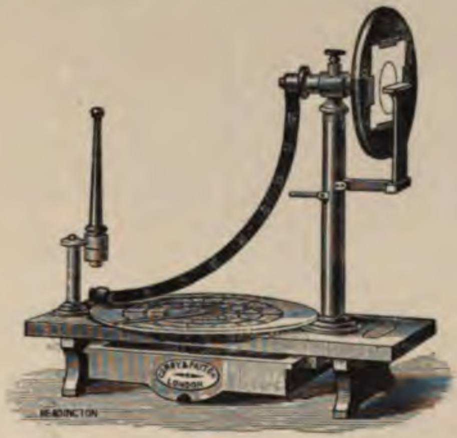

FIG. 591.—Priestley Smith's Perimeter.

Fig. 591 shows one of the forms of perimeter very generally employed, and fig. 592 represents one of the charts provided with the instrument. The blind spot is shown, and the dotted line represents the normal average field of vision for the right eye.

It will be seen that the field of vision is most extensive on the outer side; it is less on the inner side because of the presence of the nose.

By the use of the same instrument, it is found that the colour of a coloured object is not distinguishable at the margin, but only towards the centre of the field of vision, but there are differences for different colours; thus a blue object is seen to be blue over a wider field than a red, and a red over a wider field than a green object.

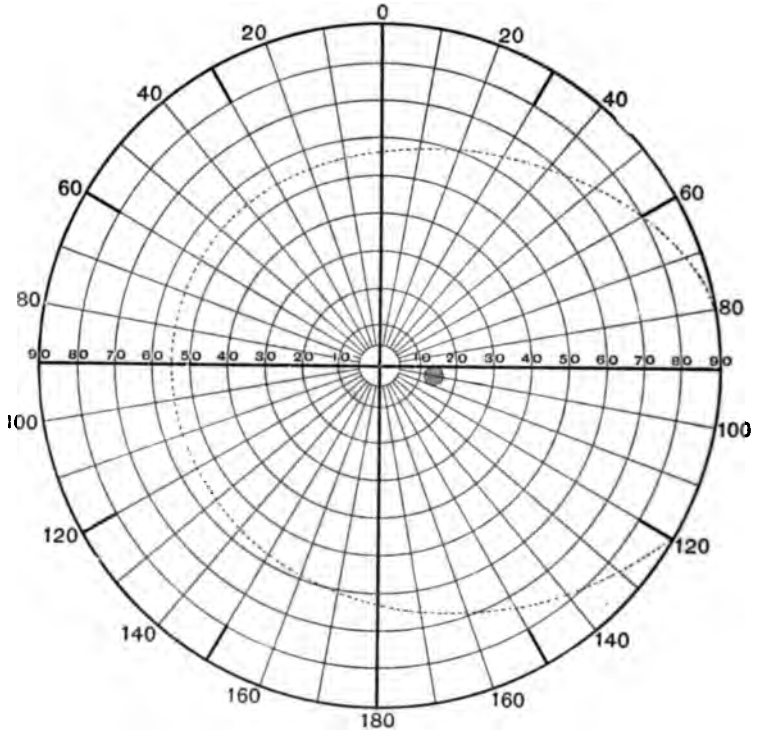

FIG. 592.—Perimeter chart for the right eye.

In disease of the optic nerve, contraction of the field of vision for white and coloured objects is found. This is often seen before any change in the optic nerve is discoverable by the ophthalmoscope.

The yellow spot of one's own eye can be rendered evident by what is called Clerk-Maxwell's experiment:—On looking through a solution of chrome-alum in a bottle with parallel sides, an oval purplish spot is seen in the green colour of the alum. This is due to the pigment of the yellow spot.

Colour Sensations.

Colours may differ (1) in *hue*, for instance, blue, red, yellow; (2) in *saturation*, for instance, pale green and full green; this depends upon the degree of admixture with white light; and (3) in *intensity*, *i.e.*, the amount of light per unit area of surface. These differences are dependent respectively on the length, the purity, and the amplitude of the light-wave. Colours also differ (4) in *brightness* or *luminosity*; this is a purely physiological quality devoid of any known physical counterpart. The brightness of a colour may be measured by determining the shade of grey to which it appears equivalent. Even the most saturated colours (for instance, yellow and blue) have different degrees of brightness varying with change of illumination (see also p. 803).

If a ray of sunlight is allowed to pass through a prism, it is decomposed by its passage into rays of different colours, which are called the colours of the spectrum; they are red, orange, yellow, green, blue, indigo, and violet. The red rays are the least turned out of their course by the prism, and the violet the most, whilst the other colours occupy in order places between these two extremes. The differences in the colour of the rays depend upon the rapidity of vibrations producing each, the red rays being the least rapid and the violet the most. In addition to these, there are others which are invisible but which have definite properties; those to the left of the red are less refrangible, being the calorific rays which act upon the thermometer, and those to the right of the violet, which are called the actinic or chemical rays, have a powerful chemical action.

White light may be built from its constituents in several ways, for instance, by a second prism reversing the dispersion produced by the first, or by causing the colours of the spectrum to fall on the retina in rapid succession. The best way to study the effects of mixing colour sensations is by means of a rapidly revolving disc to which two or more coloured sectors are fixed. Each colour is viewed in rapid succession, and owing to the persistence of retinal impressions, the constituent colour impressions blend and give a single sensation of colour. (Maxwell.)

White light can be produced by the mixture of the three primary colours, or even of two colours in certain hues and proportions. These pairs of colours, of which red and greenish-blue, orange and blue, and violet and yellow are examples, are called *complementary*.

The colours are not of equal stimulation energy, otherwise they might be arranged around a circle; they are more properly arranged in a triangle, with red, green, and violet at the angles (fig. 593). The red, green, and violet are selected on the theory of Helmholtz that they constitute the three primary colour sensations; other colour sensations are mixtures of these.

Thus, the orange and yellow between the red and green are mixtures of the red and green sensations; the blue a mixture of green and violet; and the purples (which are not represented in the spectrum) of red and violet.

Join the three angles red, green, and violet, and one gets white light; or join the blue and orange, which comes to the same thing, and one also gets white.

Blue and orange on Maxwell's disc give white; but it is well known that a mixture of blue and orange paint gives green; how can one explain this? Suppose the paint is laid on white paper; the white light from the paper on its way to the eye passes through transparent particles of blue and orange pigment; the blue particles only let the green and violet sensations reach the eye, and cut off the red; the yellow particles only let the red and green through, and cut off the violet. The red and violet being thus cut off, the green sensation is the only one which reaches the eye.

The experiments which led Helmholtz and others to the selection of green, red, and violet as the three fundamental colour sensations were performed in this way: the eye undergoes exhaustion to a colour when exposed to it for some time; suppose, for instance, the eye is fatigued for red, and is then exposed to a pure yellow light, such as that given off by the sodium flame, the yellow then appears greenish; or fatigue the eye for green and then expose it to blue, the blue will have a violet tint. By the repetition of numerous experiments of this kind, it was found that the fatigue experienced manifested itself in three colours, red, green, and violet, which were therefore selected as the three fundamental colour sensations. It was also found that these three colour sensations could not be produced by any combination of other colour sensations, and further that all other colour sensations can be obtained by mixing these three in various proportions.

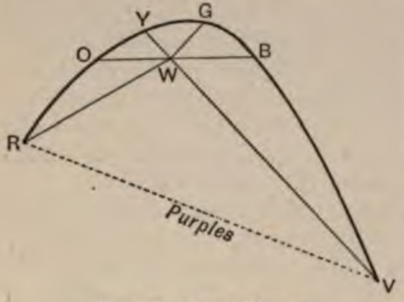

FIG. 593.—Colour triangle.

The theory of colour vision constructed on these data was originated by Thomas Young, and independently discovered and elaborated by Helmholtz. It is consequently known as the Young-Helmholtz theory. This theory teaches that there are in the retina certain elements (? cones) which answer to each of these primary colours, whereas the innumerable intermediate shades of colour are produced by stimulation of the three primary colour terminals in different degrees, the sensation of white being produced when the three elements are equally excited. Thus, if the retina is stimulated by rays of certain wave length, at the red end of the spectrum, the terminals of the other colours, green and violet, are hardly stimulated at all, but the red terminals are strongly stimulated, the resulting sensation being red. The orange rays excite the red terminals considerably, the green rather more, and the violet slightly, the resulting sensation being that of orange, and so on (fig. 594).

Another theory of colour vision (Hering's) supposes that there are six primary colour sensations, viz.: three pairs of antagonistic colours, black and white, red and green, and yellow and blue; and that these are produced by the changes either of disintegration or of assimilation taking place in certain substances, somewhat, it may be supposed, of the nature of the visual purple, which (the theory supposes) exist in the retina. Each of the substances corresponding to a pair of colours is capable of undergoing two changes, one of construction and the other of disintegration, with the result of producing one or other colour. For instance, in the white-black substance, when disintegration is in excess of construction or assimilation, the sensation is white, and when assimilation is in excess of disintegration the reverse is the case; and similarly with the red-green substance, and with the yellow-blue substance. When the repair and disintegration are equal with the first substance, the visual sensation is grey; but in the other pairs, when this is the case, no sensation occurs. The rays of the spectrum to the left produce changes in the red-green substance only, with a resulting sensation of red, whilst the (orange) rays further to the right affect both the red-green and the yellow-blue substances; blue rays cause constructive changes in the yellow-blue substances, but none in the red-green, and so on. These changes produced in the visual substances in the retina are perceived by the brain as sensations of colour.

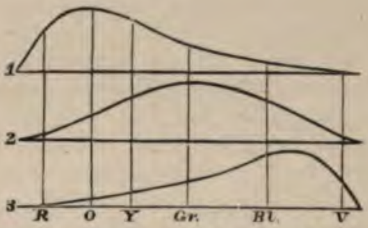

FIG. 594.—Diagram of the three primary colour sensations. (Young-Helmholtz theory.) 1 is the red; 2, green, and 3, violet, primary colour sensation. The lettering indicates the colours of the spectrum. The diagram indicates by the height of the curve to what extent the several primary sensations of colour are excited by vibrations of different wave lengths.

Neither theory satisfactorily accounts for all the numerous complicated problems presented in the physiology of colour vision. One of these problems is *colour blindness*, a by no means uncommon visual defect. Some people are completely colour blind, but the commonest form is the inability to distinguish between red and green. Helmholtz's explanation of such a condition is, that the elements of the retina which receive the impression of red, etc., are absent, or very imperfectly developed, and Hering's would be that the red-green substance is absent from the retina. Other varieties of colour-blindness in which the other colour-perceiving elements are absent, have been shown to exist occasionally.

Hering's theory appears to meet the difficulty best, for if the red element of Helmholtz were absent, the patient ought not to be able to perceive white sensations, of which red is a constituent part; whereas, according to Hering's theory, the white-black visual substance remains intact. It likewise explains to some extent the phenomena of total colour blindness, which is an almost inconceivable condition, if the Young-Helmholtz theory is accepted.

These two theories have been for a long time before the scientific world. As facts have accumulated, it has been for some years recognised that many facts could not be reconciled with either; and modifications of one or the other have been from time to time introduced.

The observations made by C. J. Burch are of considerable importance: the following is a brief account of his methods and results.

He finds that by exposing the eye to bright sunlight in the focus of a burning glass behind transparent coloured screens, it is possible to produce temporary colour blindness. After red light, the observer is for some minutes red-blind, scarlet geraniums look black, yellow flowers green, and purple flowers violet. After violet light, violet looks black, purple flowers crimson, and green foliage richer than usual. After light of other colours, corresponding effects are produced. If one eye is made purple-blind, and the other green-blind, all objects are seen in their natural colours, but in exaggerated perspective, due to the difficulty the brain experiences in combining the images from the two eyes.

By using a brightly-illuminated spectrum, and directing the eye to certain of its colours, the eye in time becomes fatigued and blind for that colour, so that it is no longer seen in the spectrum. Thus, after green blindness is induced the red appears to meet the blue, and no green is seen. If, however, the eye is exposed to yellow light, it does not similarly become blind for yellow only, but for red and green too. This supports the Young-Helmholtz theory, that the sensation yellow is one compounded of the red and green sensations. By an exhaustive examination of the different parts of the spectrum, in this way it thus becomes possible to differentiate between the primary colour sensations and those which are compound. By a study of this kind, Burch concludes that the phenomena of colour vision are in accordance with the Young-Helmholtz theory, with the important addition that there is a fourth primary colour sensation, namely, blue. He could not discover that colour sensations are related to each other in the sense indicated by Hering. Each may be exhausted without either weakening or strengthening the others. These observations were confirmed by examining in a similar way the colour sensations of seventy other people, but there are individual differences in the extent to which the colour sensations overlap.

After-Images.—These are the after-effects of retinal excitation, and are divided into *positive* and *negative*. Positive after-images resemble the original image in distribution of brightness and colour. In negative after-images bright parts appear dark, dark parts bright, and coloured parts in the complementary or contrast colours.

If a bright white object is looked at, and the eyelids are then closed, a positive after-image is seen which fades gradually, but as it fades it passes through blue, violet or red, to orange; according to the Young-Helmholtz theory, this is explained on the hypothesis that the excitation does not decline with equal rapidity in the three colour terminals. Further details of these after-images are given on p. 803. A positive after-image is readily obtained by momentarily looking at a bright object, *e.g.* a window, after waking from sleep. Negative after-images develop later than positive images, and may be seen either by closing the eyes or by turning them to a uniform grey surface after viewing an object steadily.

If the object looked at is coloured, the negative after-image seen upon such a background is in its complementary colour; this is explained by the Young-Helmholtz theory, by the supposition that the colour perceiving element for the colour looked at is the most fatigued, and the terminals for its complementary colour least fatigued. On the Hering theory, one colour produces anabolic or katabolic effects as the case may be; on withdrawing the eye from stimulation by that particular colour, the opposite phase of metabolism takes place and produces the complementary colour. One has an analogy to this in the case of the heart; when that organ has been thrown into an anabolic state by the stimulation of the vagus, it will beat better when the stimulation stops owing to increase of katabolic processes.

Negative after-images are frequently spoken of as phenomena of ***successive contrast***. Somewhat more complex than these are the phenomena of ***simultaneous contrast***. A white object looks whiter when viewed against a dark background than when seen against a white background; the colour of an object is intensified by viewing it against a background of its complementary hue. Another familiar experiment is the following:—A piece of grey paper is placed on a green sheet, and the whole covered with tissue paper; the grey patch then appears to be reddish, that is, of the colour complementary to green. Helmholtz regarded such phenomena as the result of false judgment, and not of changes in excitability of the different parts of the retina.* It certainly appears easier to explain contrast by the Hering theory; excitation by one colour induces an opposite metabolic process in neighbouring areas of the retina; if two stimuli of opposite character are presented simultaneously side by side, the contrast effect will be most marked. In the experiment with tissue paper, the greater part of the retina is being excited by green, and the part of the retina stimulated by the feeble white light from the grey paper will undergo the opposite change and produce a sensation of red.

By means of the stereoscope, binocular combinations of colour can be obtained. Thus, if one eye is exposed to a red disc, and the corresponding portion of the other eye to a yellow one, the mind usually perceives one disc of an orange tint; but frequently, especially if there be differences of brightness or of form in the two objects, we notice that "rivalry of the fields of vision" occurs, first one then the other disc rising into consciousness. A stereoscopic combination of black and white produces the appearance of metallic lustre; this is very beautifully shown with figures of crystals, one black on a white ground, the other white on a black ground. Probably the combination of black and white is interpreted as indicating a polished surface, because a polished surface reflects rays irregularly so that the two eyes receive stimuli of unequal intensity.

Changes in the Retina during Activity.

The method by which a ray of light is able to stimulate the endings of the optic nerve in the retina in such a manner that a visual sensation is perceived by the cerebrum, is not yet understood. It is supposed that the change effected by the agency of the light which falls upon the retina is in fact a chemical alteration in the protoplasm, and that this change stimulates the optic nerve-endings. The discovery of a certain temporary reddish-purple pigmentation of the outer limbs of the retinal rods in certain animals (*e.g.*, frogs) which had been killed in the dark, forming the so-called *rhodopsin or visual purple*, appeared likely to offer some explanation of the matter, especially as it was also found that the pigmentation disappeared when the retina was exposed to light, and reappeared when the light was removed, and also that it underwent distinct changes of colour when other than white light was used. It was also found that if the operation were performed quickly enough, the bleached image of a bright object (*optogram*) might be fixed on the retina by soaking the retina of an animal which has been killed in the dark, in alum solution.

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* By "retina" here and elsewhere we mean "cerebro-retinal apparatus." We have no knowledge of the precise share of retina and brain in the development of visual sensations and after-sensations.

The rhodopsin is derived in some way from the black pigment (melanin or fuscin) of the polygonal epithelium of the retina, since the colour is not renewed after bleaching if the retina is detached from its pigment layer.

Certain pigments, not sensitive to light, are contained in the inner segments of the cones. These are oil globules of various colours, red, green, and yellow, called *chromophanes*, and are found in the retinæ of marsupials (but not other mammals), birds, reptiles, and fishes. Nothing is known about the yellow pigment of the yellow spot.

Another change produced by the action of the light upon the retina is the *movement of the pigment cells*. On being stimulated by light the granules of pigment in the cells which overlie the outer part of the rod and cone layer of the retina pass down into the processes of the cells, which hang down between the rods: these *melanin* or *fuscin* granules are generally rod-shaped, and look almost like crystals. In addition to this, a *movement of the cones* and possibly of the rods occurs, as has been already mentioned; in the light the cones shorten, and in the dark they lengthen (Engelmann).

Dewar and McKendrick were the first to show that the chemical changes in the retina are accompanied with an electrical change.

Red light has no action on visual purple; the maximum bleaching effect takes place in greenish-yellow light. Now, when the living eye is brought into a condition of "dark adaptation," that is, when the retina has become adapted to light of low intensity, the colours of the spectrum alter in brightness; the red end becomes shortened and much darker; the blue end becomes brighter, and the region of maximum brightness is in the green. This change of brightness with change of adaptation is absent in the fovea, where there are no rods. The selective action of the colours of the spectrum on the visual purple is so strikingly similar to the altered conditions of brightness just described, that changes in the visual purple of the rods have been supposed to be the cause of sensations excited by feeble illumination (*i.e.*, in the "dark-adapted" eye), while the cones are affected under more ordinary conditions of illumination. This conclusion gains support from several interesting facts. Visual purple is specially abundant in the retinæ of almost all animals whose habits are nocturnal, or who live underground. Further, if the intensity of a colour stimulus is gradually increased, it at first is too faint to produce any sensation; then it produces a sensation of greyness, and at last the colour itself is seen; the interval between the appearance of the grey or white-black effect and of the true colour effect of the stimulus is spoken of as the "*photo-chromatic interval.*" Red light has no effect on visual purple, and has no photo-chromatic interval (that is, it appears either red or nothing), and according to several observers, there is no such interval at the fovea, where the rods and therefore visual purple, are absent. Thirdly, a very similar effect has been described by M'Dougall, when the retina is momentarily stimulated by a coloured light; the sensation arising from the stimulus is followed by a series of "primary responses" or after-sensations; the first members of the series have the same colour as the stimulus, and these are sometimes followed by a series of colourless (grey) sensations; these grey sensations are only present outside the fovea, and under conditions of "dark adaptation" are absent with red and brightest with green stimuli. Here again we are able to differentiate between a visual-purple (rod) effect, and a cone effect, the former, active under conditions of feeble illumination, affected most by green, and unaffected by red light, and yielding colourless sensations; the latter being more specially concerned in developing sensations of colour under conditions of adaptation to ordinary light. The fovea centralis thus becomes the region where the colours of objects are best distinguishable, and where with ordinary illumination visual acuity is most marked. In the dark, however, extra-foveal (rod) vision is more sensitive than foveal (cone) vision; astronomers see faint stars more readily in the periphery of the field of vision.

Two abnormal conditions may be described here, for they throw light on these phenomena. In cases of *achromatopsia* (total colour blindness) the spectrum is seen as a band of light differing only in brightness; the region of maximum brightness is the same as in extra-foveal vision of the normal eye; in many of these cases there is a central *scotoma* (blind spot), that is, the rod-less fovea is blind; there is reduced acuity of vision as in the "dark-adapted" eye, and *photophobia* (fear of strong light); *nystagmus* (oscillating movements of the eye) also occurs due to absence of an area of distinct vision. We are thus in typical cases of achromatopsia dealing with cases of cone blindness. In *nyctalopia* (night blindness) on the other hand, we meet the converse condition. Here there is an abnormal slowness of "dark adaptation," and a pathological change known as *retinitis pigmentosa* is present, suggesting an impaired function of the visual purple. Pilocarpine has been found an effective drug in such cases, and this is also interesting because it hastens the regeneration of visual purple in the extirpated eye.

The electrical variations in the retina under the influence of light have been recently reinvestigated by Waller. The excised eyeball of a frog is led off by non-polarisable electrodes to a galvanometer. One electrode is placed on the front, the other on the back of the eye. If the eyeball is quite fresh, a current is observed passing through the eyeball from back to front. When light falls on the eye this current is increased; on shutting off the light there is a momentary further increase, and then the current slowly returns back to its previous condition. Waller explains this by supposing that anabolic changes in the eye predominate during stimulation by light. With the onset of darkness, the katabolic changes cease at once, and the anabolic more slowly; hence a further positive variation.

As already stated, the current in a fresh eyeball passes from back to front before the stimulus is applied, but this cannot be regarded as a true current of rest, but as a current due to previous action which very slowly subsides. When this has subsided, the true current of rest is from cornea to fundus, *i.e.*, it is like that of the skin (see p. 473) ingoing—the response to stimulation is like that of the skin outgoing. Waller has also studied the electrical responses of the eyeball to other methods of stimulation; if electrical currents are employed, and the eyeball is still healthy, the response is always an outgoing current, whatever may be the direction of the electrical current used as the stimulus. These currents of action are no doubt mainly of retinal origin, but later Waller showed that the anterior portions of the eye, especially the crystalline lens, participate in their causation. The response of the eye to non-luminous stimuli lasts some time, and is spoken of as a "blaze current." An analogous response has been seen in skin, plant-tissues, etc.

Gotch has studied the photo-electric changes in the frog's eyeball with the capillary electrometer. He, like Waller, draws attention to the long latent period and sustained character of the response. The photo-electric changes are all monophasic effects, whether produced by illumination, or by shutting off the light. Gotch suggests there are two chemical substances in the retina, one of which reacts to light, the other to darkness. Each reaction is a change of the same type, but for the change to occur markedly, the eye must be previously adapted, *i.e.*, the substances must undergo a phase of metabolism under conditions opposite to those which evoke the reaction effects. Observations with red and green light do not support the view that the photo-chemical changes are of opposite characters, for the photo-electric change is always in the same direction, differing only in period of latency, that for red being the longer.

MOVEMENTS OF THE EYEBALL

Protrusion of the eyeballs occurs (1) when the blood-vessels of the orbit are congested; (2) when contraction of the plain muscular fibres of the capsule of Tenon takes place; these are innervated by the cervical sympathetic nerve; and (3) in the disease called exophthalmic goitre.

Retraction occurs (1) when the lids are closed forcibly; (2) when the blood-vessels of the orbit are comparatively empty; (3) when the fat in the orbit is reduced in quantity, as during starvation; and (4) on section or paralysis of the cervical sympathetic nerves.

The most important movements, however, are those produced by the six ocular muscles.

The internal rectus turns the eyeball inwards, the external rectus turns it outwards. If the superior rectus acted alone, it would turn the eyeball not only upwards, but owing to the sloping direction of the muscle, the eyeball would be turned inwards also; in turning the eyeball directly upwards, this inward movement is arrested by the outward tendency of the inferior oblique. Similarly, in turning the eyeball directly downwards, the inferior rectus acts in conjunction with the superior oblique. Movements in intermediate directions are produced by other combinations of the muscles.

These muscles are all supplied by the third nerve except the superior oblique, which is supplied by the fourth and the external rectus by the sixth nerve. (See p. 640.)

The muscles of the two eyes act simultaneously, so that images of the objects looked at may fall on corresponding points of the two retinæ. The inner side of one retina corresponds to the outer side of the other, so that any movement of one eye inwards must be accompanied by a movement of the other eye outwards. If one eyeball is forcibly fixed by pressing the finger against it so that it cannot follow the movement of the other, the result is double vision (*diplopia*), because the image of the objects looked at will fall on points of the two retinæ which do not correspond. The same is experienced in a squint, until the brain learns to disregard the image from one eye.

If the external rectus is paralysed, the eye will squint inwards; if this occurs in the right eye the false image will lie on the left side of the yellow spot, and appear in the field of vision to the right of the true image. If the third nerve is paralysed, the case is a more complicated one: owing to the paralysis of the levator palpebræ superioris, the patient will be unable to raise his upper lid (*ptosis*), and so in order to see will walk with his chin in the air. If the paralysis is on the right side, the eyeball will squint downwards and to the right; the false image will be formed below and to the right of the yellow spot, and the apparent image in the field of vision will consequently appear above and to the left of the true image, and owing to the squint being an oblique one, the false image will slant in a corresponding direction.

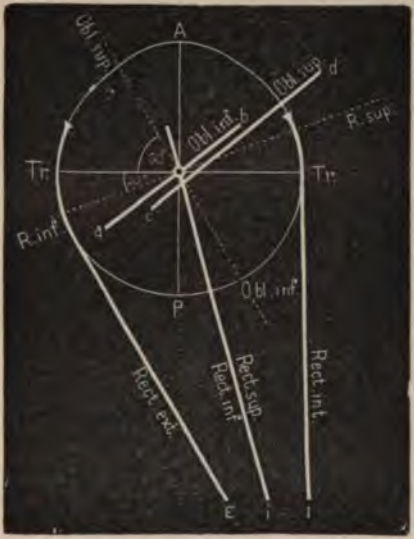

FIG. 595.—Diagram of the axes of rotation to the eye. The thin lines indicate axes of rotation, the thick the position of muscular attachment.

Various Positions of the Eyeballs.

All the movements of the eyeball take place around the *point of rotation*, which is situated 1·77 mm. behind the centre of the visual axis, or 10·9 mm. behind the front of the cornea.

The three axes around which the movements occur are:—

1. The *visual* or antero-posterior axis. (A P, fig. 595).

2. The *transverse* axis, which connects the points of rotation of the two eyes. (Tr, fig. 595).

3. The *vertical* axis, which passes at right angles to the other two axes through their point of intersection.

The line which connects the fixed point in the outer world at which the eye is looking to the point of rotation is called the *visual line.* The plane which passes through the two visual lines is called the *visual plane.*

The various positions of the eyeballs are designated primary, secondary, and tertiary.

The *primary* position occurs when both eyes are parallel, the visual lines being horizontal (as in looking at the horizon).

Secondary positions are of two kinds:—

(1) The visual lines are parallel, but directed either upwards or downwards from the horizontal (as in looking at the sky).

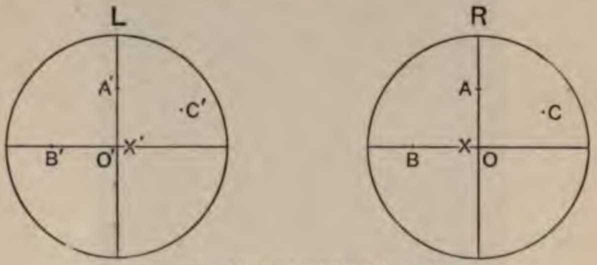

FIG. 596.—Identical points of the retinæ.

(2) The visual lines are horizontal, but converge towards one another (as in looking at a small object near to and immediately on the same level as the eyes).

Tertiary positions are those in which the visual lines are not horizontal, and converge towards one another (as in looking at the tip of the nose).

It is possible to conceive positions of the eyeballs in which the visual lines diverge from one another; but such positions do not occur in normal vision in man.

Both eyes are moved simultaneously, even if one of them happens to be blind. They are moved so that the object in the outer world is focussed on the two yellow spots, or other corresponding points of the two retinæ. The images which do not fall on corresponding points are seen double, but these are to a great extent disregraded by the brain, which pays particular attention to those images which fall on corresponding points.

The accompanying diagrams will assist us in understanding what is meant by *corresponding* or *identical* points of the two retinæ.

If R and L (fig. 596) represent the right and left retinæ respectively, O and O′ the two yellow spots are identical; so are A and A′, both being the same distance above O and O′. But the corresponding point to B on the inner side of O in the right retina, is B′, a point to the same distance on the outer side of O′ in the left retina; similarly C and C′ are identical. The two blind spots X and X′ are not identical.

Fig. 597 shows the same thing in rather a different way; A and B represent a horizontal section through the two retinæ; the points a a′, b b′, and c c′, being identical. In the lower part of the diagram is shown the way in which the brain combines the images in the two retinæ, one overlapping so as to coincide with the other.

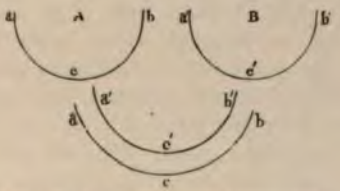

FIG. 597.—Diagram to show the corresponding parts of both retinæ.

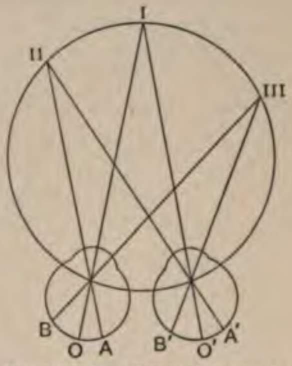

FIG. 598.—The Horopter, when the eyes are convergent.

The *Horopter* is the name given to the surface in the outer world which contains all the points which fall on the identical points of the retinæ. The shape of the horopter will vary with the position of the eyeballs. In the primary position, and in the first variety of the secondary position, the visual lines are parallel; hence the horopter will be a plane at infinity, or at a great distance.

In the other variety of the secondary position, and in tertiary positions in which the visual lines converge, as when looking at a near object, the horopter is a circle (fig. 598) which passes through the nodal points of the two eyes, and through the fixed point (I) in the outer world at which the eyes are looking, and which will consequently fall on the two yellow spots (O and O′). All other points in this circle (II, III) will fall on identical points of the retinæ. The image of II will fall on A and A′; of III on B and B′; it is a simple mathematical problem to prove that $OA = O'A'$, and $OB = O'B'$.

This, however, applies to man only, or to animals with both eyes in front of the head; in those animals in which the eyes are lateral in position, and the visual lines diverge, the problem of binocular vision is a very different one (see also p. 713).

Nervous Paths in the Optic Nerves.

The correspondence of the two retinæ and of the movements of the eyeballs is produced by a close connection of the nervous centres controlling these phenomena, and by the arrangement of the nerve-fibres in the optic nerves. The crossing of the nerve-fibres at the optic chiasma is incomplete, and the next diagram (fig. 599) gives a simple idea of the way the fibres go.

It will be seen that it is only the fibres from the inner portions of the retinæ that cross; and that those represented by continuous lines from the right side of the two retinæ ultimately reach the right hemisphere, and those represented by interrupted lines from the left side of the two retinæ ultimately reach the left hemisphere. The two halves of the retinæ are not, however, separated by a hard-and-fast line from one another; this is represented by the two halves being depicted as slightly overlapping, and this comes to the same thing as saying that the central region of each retina is represented in each hemisphere.

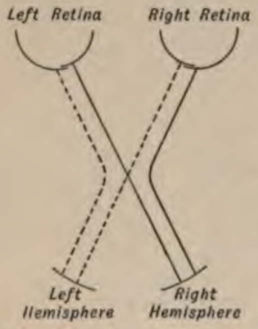

FIG. 599.—Course of fibres at optic chiasma.

The part of the hemisphere concerned in vision is the occipital lobe, and the reader should turn back to our previous consideration of this subject in connection with cerebral localisation, the phenomena of hemianopsia (p. 689) and the conjugate deviation of head and eyes (pp. 689, 703).

Fig. 600, though diagrammatic, will assist the reader in more fully comprehending the paths of visual impulses, and the central connections of the nerves and nerve-centres concerned in the process. The fibres to the external geniculate body end there by arborising around its cells, and a fresh relay of fibres from these cells passes in the posterior part of the internal capsule to the cortex of the occipital lobe. Those to the anterior corpus quadrigeminum are continued on by a fresh relay to the nuclei of the nerves concerned in eye-movements (represented by the oculo-motor nucleus in the diagram); the axons of the cortical cells pass to the tegmentum, whence a fresh relay continues the impulse to the oculo-motor nucleus.

Visual Judgments.

The psychical or mental processes which constitute the visual sensation proper have been studied to a far greater degree than is possible in connection with other forms of sensation.

We have already seen that in spite of the reversion of the image in the retina, the mind sees objects in their proper position; this is explained on p. 780.

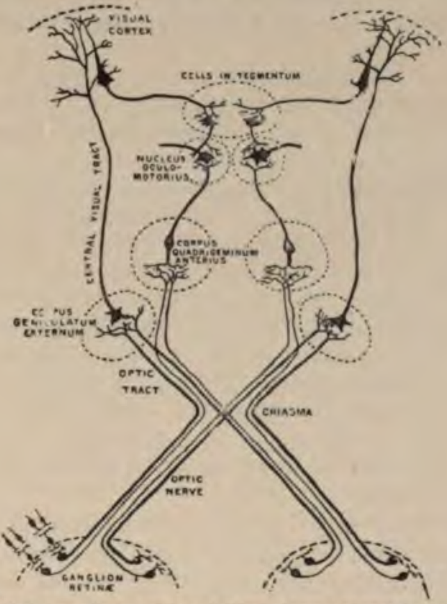

FIG. 600.—Relations of nerve cells and fibres of visual apparatus. (Schäfer.)

We are also not conscious of the blind spot. This is partly due to the fact that those images which fall on the blind spot of one eye are not focussed there in the other eye. But even when one looks at objects with one eye, there is no blank, for the reason explained on p. 790.

Our estimate of the size of various objects is based partly on the visual angle (p. 779) under which they are seen, but much more on the estimate we form of their distance. Thus a lofty mountain many miles off may be seen under the same visual angle as a small hill near at hand, but we infer that the former is much the larger object because we know it is much farther off than the hill. Our estimate of distance is often erroneous, and consequently the estimate of size also. Thus persons seen walking on the top of a small hill against a clear twilight sky appear unusually large, because we over-estimate their distance, and for similar reasons most objects in a fog appear immensely magnified. The same mental process gives rise to the idea of depth in the field of vision; this idea is fixed in our mind principally by the circumstance that, as we ourselves move forwards, different images in succession become depicted on our retina, so that we seem to pass between these images, which to the mind is the same thing as passing between the objects themselves.

The action of the sense of vision in relation to external objects is, therefore, quite different from that of the sense of touch. The objects of the latter sense are immediately present to it; and our own body, with which they come in contact, is the measure of their size. The part of a table touched by the hand appears as large as the part of the hand receiving an impression from it, for the part of our body in which a sensation is excited, is here the measure by which we judge of the magnitude of the object. In the sense of vision, on the contrary, the images of objects are mere fractions of the objects themselves, realised upon the retina, the extent of which remains constantly the same. But the imagination, which analyses the sensations of vision, invests the images of objects, together with the whole field of vision in the retina, with very varying dimensions; the relative size of the image in proportion to the whole field of vision, or of the affected parts of the retina to the whole retina, alone remains unaltered.

The estimation of the form of bodies by sight is the result partly of the mere sensation, and partly of the association of ideas. Since the form of the images perceived by the retina depends wholly on the outline of the part of the retina affected, the sensation alone is adequate to the distinction of superficial forms from each other, as of a square from a circle. But the idea of a solid body like a sphere, or a cube, can only be attained by the action of the mind constructing it from the different superficial images seen in different positions of the eye with regard to the object, and, as shown by Wheatstone and illustrated in the *stereoscope,* from two different perspective projections of the object being presented simultaneously to the mind by the two eyes.

Thus, if a cube is held at a moderate distance before the eyes, and viewed with each eye successively while the head is kept perfectly steady, A (fig. 601) will be the picture presented to the right eye, and B that seen by the left eye. Wheatstone has shown that on this circumstance depends in a great measure our conviction of the solidity of an object, or of its projection in relief. If different perspective drawings of a solid body, one representing the image seen by the right eye, the other that seen by the left (for example, the drawing of a cube, A, B, fig. 601) be presented to corresponding parts of the two retinæ, as may be readily done by means of the stereoscope, the mind will perceive not merely a single representation of the object, but a body projecting in relief, the exact counterpart of that from which the drawings were made.

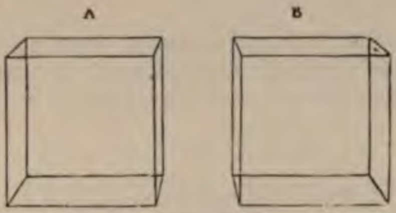

FIG. 601.—Diagrams to illustrate how a judgment of a figure of three dimensions is obtained.

By transposing two stereoscopic pictures a reverse effect is produced; the elevated parts appear to be depressed, and *vice versâ.* An instrument contrived with this purpose is termed a *pseudoscope.* Viewed with this instrument a bust appears as a hollow mask, and as may readily be imagined the effect is most bewildering.

The clearness with which the details of an object is perceived irrespective of accommodation, would appear to depend largely on the number of rods and cones which its retinal image covers. Hence the nearer an object is to the eye (within moderate limits) the more clearly are all its details seen. Moreover, if we want carefully to examine any object, we always direct the eyes straight to it, so that its image shall fall on the two yellow spots, where an image of a given area will cover a larger number of cones than anywhere else in the retina. Moreover, as previously pointed out, each cone in the macula lutea is connected to a separate chain of neurons.

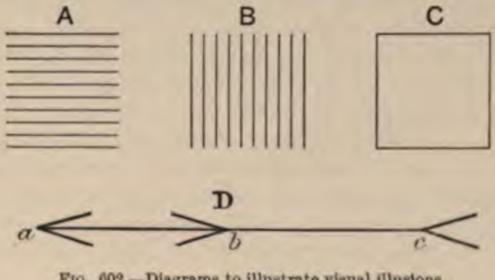

FIG. 602.—Diagrams to illustrate visual illusions.

The importance of binocular vision is very great. If an object is looked at with one eye only, it is impossible to estimate its distance by the sense of vision alone. For instance, if one eye is closed and the other looks at a wire or bar, it is impossible to tell whether, if some one drops a small object, it falls in front of or behind the bar.

Visual judgments are not always correct; there are a large number of puzzles and toys which depend on visual illusions. One or two of the best known are represented in the accompanying diagrams.

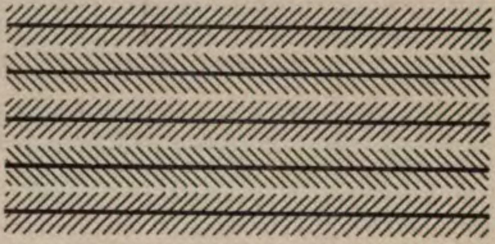

FIG. 603.—Parallel puzzle.

In fig. 602, A, B, and C are of the same size; but A looks taller than B, while C appears to cover a less area than either. The subdivision of a space or line increases its apparent size or length. In fig. 602 D, *ab* is equal to *bc*. Vertical distances also are usually over-estimated.

In fig. 603, the horizontal lines are parallel, though they do not appear so, owing to the mind being distracted by the intercrossing lines.

CHAPTER LVII

TROPHIC NERVES

NERVES exercise a trophic or nutritive influence over the tissues and organs they supply. Some nerves increase the building-up stage of metabolism; these are termed anabolic. Such a nerve is the vagus in reference to the heart; when it is stimulated the heart beats more slowly or may stop, and is thus enabled to rest and repair its waste. The opposite kind of nerves (katabolic) are those which lead to increase of work, and so increased wear and tear and formation of waste products. Such a nerve in reference to the heart is the sympathetic.

There has been considerable diversity of opinion as to whether trophic nerve-fibres are a distinct anatomical set of nerve-fibres, or whether all nerves in addition to their other functions exercise a trophic influence.

When a nerve going to an organ is cut, the wasting of the nerve itself beyond the cut constitutes what we have learnt to call Wallerian degeneration, but the wasting process continues beyond the nerve; the muscles it supplies waste also, and waste much more rapidly than can be explained by simple disuse. The same is seen in the testicle after section of the spermatic cord; and in the disease of joints called Charcot's disease, the trophic changes are to be explained by disease of the nerves supplying them.

From these, and numerous other instances that might be given, there is no question that nerves do exert a trophic influence; the question, however, whether this is due to special nerve-fibres has been chiefly worked out in connection with the fifth cranial nerve.

After the division of this nerve there is loss of sensation in the corresponding side of the face: the cornea in two or three days begins to get opaque, and this is followed by a slow inflammatory process which may lead to a destruction not only of the cornea, but of the whole eyeball. The same is seen in man; when the fifth nerve is diseased or pressed upon by a tumour beyond the Gasserian ganglion, the result is loss of sensation in the face and conjunctiva, an eruption (*herpes*) appears on the face, and ulceration of the cornea leading in time to disintegration of the eyeball may occur too. In disease such as hæmorrhage in the spinal ganglia there is a similar herpetic eruption on the skin (*shingles*).

In the case of the fifth nerve the evidence that there are special nerve-fibres to which these trophic changes are due, is an experiment by Meissner and Büttner, who found that division of the most internal fibres is most potent in producing them.

Those, however, who do not believe in special trophic nerves, attribute the changes in the eyeball to its loss of sensation. Dust, etc., is not felt by the cornea, and is therefore allowed to accumulate and set up inflammation. This is supported by the fact that if the eyeball is protected by sewing the eyelids together the trophic results do not ensue. On the other hand, in paralysis of the seventh nerve, the eyeball is much more exposed, and yet no trophic disorders follow.

Others have attributed the change to increased vascularity due to disordered vaso-motor changes; against this is the fact that in disease of the cervical sympathetic, the disordered vaso-motor phenomena which ensue do not lead to the disorders of nutrition we have described. Nevertheless in trophic disorders, it is very difficult to be sure that the disordered metabolism is not in part due to vascular disturbances.

There can, therefore, be but little doubt that we have to deal with the trophic influence of nerves;* but the dust, etc., which falls on the cornea must be regarded as the *exciting* cause of the ulceration. The division or disease of the nerve acts as the *predisposing* cause. The eyeball is more than usually prone to undergo inflammatory changes, with very small provocation.

The same explanation holds in the case of the influence of the vagi on the lungs. If both these nerves are divided, the animal usually dies within a week or a fortnight from a form of pneumonia called *vagus pneumonia,* in which gangrene of the lung substance is a marked characteristic. Here the predisposing cause is the division of the trophic fibres in the pneumogastric nerves; the exciting cause is the entrance of particles of food into the air passages, which on account of the loss of sensation in the larynx and neighbouring parts are not coughed up. Another trophic disturbance that follows division of the vagi is fatty degeneration of the heart.

Many bedsores are due to prolonged confinement in bed with bad nursing; these are of slow onset. But there is one class of bedsores which are acute; these are especially met with in cases of paralysis, due to disease of the spinal cord; they come on in three or four days after the onset of the paralysis in spite of the most careful attention; they cannot be explained by vaso-motor disturbance, nor by loss of sensation; there is, in fact, no doubt they are of trophic origin; the nutrition of the skin is so greatly impaired that the mere contact of it with the bed for a few days is sufficient to act as the exciting cause of the sore.

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* The proof, however, that there are distinct nerve-fibres anatomically is not very conclusive.

It will be noticed that in some instances of trophic disorder the nerves which are injured are efferent; the muscular wasting that occurs when a muscular nerve is cut is the best marked example of this. In nerve itself Wallerian degeneration follows the direction of growth, which, as a rule, is the direction in which the nerve transmits impulses. The acute Wallerian change does not actually leap synapses, still the trophic influence of one set of neurons upon a second set among which the axons of the first set terminate is shown by a slow wasting process, of which chromatolysis is the principal visible sign. In the peripheral axons of the cells of the spinal and corresponding cranial ganglia, the trophic disorder follows a peripheral direction, while impulses are carried in the opposite or afferent direction. The trophic influence here travels against the stream of impulse. It cannot fail to be a striking fact that the most marked trophic disorders with which we are acquainted, herpes, acute bedsores, Charcot's disease, eye changes after division or injury to the fifth nerve, vagus pneumonia, etc., are due to interference with sensory channels. Loss of sensation is the great predisposing cause of nutritive mischief.

CHAPTER LVIII

THE REPRODUCTIVE ORGANS

THE reproductive organs consist in the male of the two testes which produce spermatozoa, and the ducts which lead from them, and in the female of the two ovaries which produce ova, the Fallopian tubes or oviducts, the uterus, and the vagina.

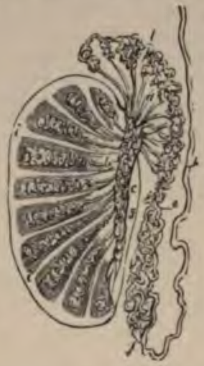

FIG. 604.—Plan of a vertical section of the testicle, showing the arrangement of the ducts. The true length and diameter of the ducts have been disregarded. *a a*, Tubuli seminiferi coiled up in the separate lobes; *b*, tubuli recti; *c*, rete testis; *d*, vasa efferentia ending in the coni vasculosi; *l*, *e*, *g*, convoluted canal of the epididymis; *h*, vas deferens; *f*, section of the back part of the tunica albuginea; *i i*, fibrous processes running between the lobes; *s*, mediastinum.

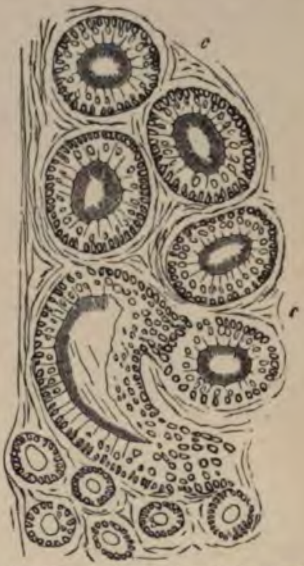

FIG. 605.—Section of the epididymis of a dog.—The tube is cut in several places, both transversely and obliquely; it is seen to be lined by a ciliated epithelium, the nuclei of which are well shown. *c*, Connective tissue. (Schofield.)

MALE ORGANS

The testis is enclosed in a serous membrane called the *tunica vaginalis*, originally a part of the peritoneum. It descends into the scrotum before the testis and subsequently gets entirely cut off from the remainder of the peritoneum. There are, however, many animals in which the testes remain permanently in the abdomen. The external covering of the testicle itself is a strong fibrous capsule, called, on account of its white appearance, the *tunica albuginea.* Passing from its inner surface are a number of septa or trabeculæ, which divide the organ imperfectly into lobules. On the posterior aspect of the organ the capsule is greatly thickened, and forms a mass of fibrous tissue called the *Corpus Highmorianum* (body of Highmore) or *mediastinum testis.* Attached to this is a much convoluted tube, which forms a mass called the *epididymis.* This receives the ducts of the testis, and is prolonged into a thick walled tube, the *vas deferens,* by which the semen passes to the urethra.

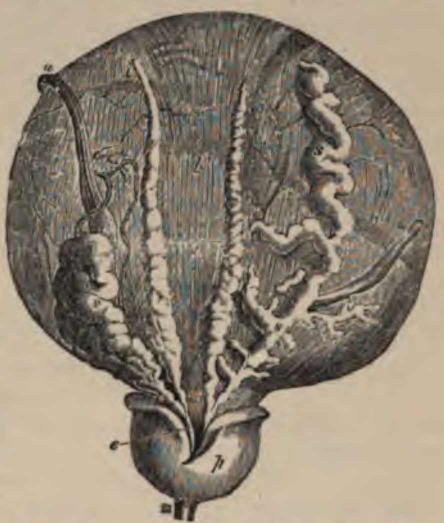

Fig. 606.—Dissection of the base of the bladder and prostate gland, showing the vesiculæ seminales and vasa deferentia. *a*, Lower surface of the bladder at the place of reflexion of the peritoneum; *b*, the part above covered by the peritoneum; *i*, left vas deferens, ending in *e*, the ejaculatory duct; the vas deferens has been divided near *i*, and all except the vesical portion has been taken away; *s*, left vesicula seminalis joining the same duct; *s s*, the right vas deferens and right vesicula seminalis, which has been unravelled; *p*, under side of the prostate gland; *m*, part of the urethra; *u u*, the ureters (cut short), the right one turned aside. (Haller.)

Each lobule of the testicle contains several *convoluted* tubes. Every tube commences near the tunica albuginea, and terminates after joining with others in a *straight tubule,* which passes into the body of Highmore, where it ends in a network of tubes, the *rete testis.* From the rete about fifteen efferent ducts (*vasa efferentia*) arise, which become convoluted to form the *coni vasculosi,* and then pass into the tube of the epididymis.

The *convoluted* or seminiferous tubes (fig. 607) have the following structure: each consists of (1) an outer boundary of flattened connective tissue cells intermingled with elastic fibres; (2) a fine membrana propria; (3) a lining epithelium of many layers of germinal cells. Next the membrana propria is a layer of cells, some of which are primordial germinal cells, others are *spermatogonia* produced from the primordial germinal cells, but differing from them in structure, and the remainder are supporting or nurse cells which provide nutriment for the developing spermatozoa. More internally, between the projecting processes of the nurse cells, are large *spermatocysts* of the first order, derived from the spermatogonia by karyokinesis and growth. Still nearer the lumen of the tube lie the spermatocysts of the second order, which are the daughter-cells of the spermatocysts of the first order, and the spermatocysts of the second order give rise by divisions to the *spermatids* which lie next the lumen. The spermatids become embedded in the inner ends of the nurse cells, where they lose their distinct cellular characters and become converted into spermatozoa. Every spermatid consists of a cell body and a nucleus with a nucleolus. In the cell body near the nucleus

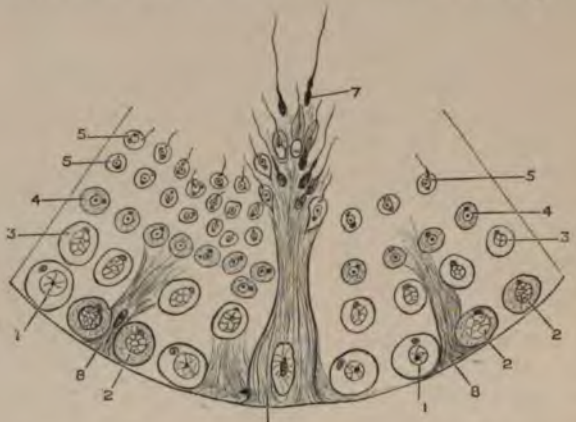

FIG. 607.—Diagram of a portion of a seminal tubule showing development of spermatozoa. 1, Primitive germ cell; 2, spermatogonia; 3, spermatocysts of the first order; 4, spermatocysts of the second order; 5, spermatids, some with commencement of axial filament; 6, a nurse cell with spermatids and spermatozoa in various stages of development; 7, free spermatozoa in lumen of tube; 8, portions of nurse cells. (After Waldeyer.)

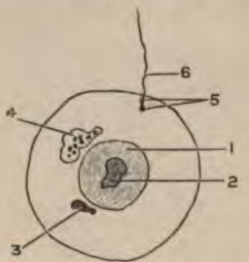

FIG. 608.—A spermatid largely magnified. 1, nucleus; 2, nucleolus; 3, chromatoid body; 4, idiosome; 5, centrosomes; 6, commencement of axial filament. (After Meves.)

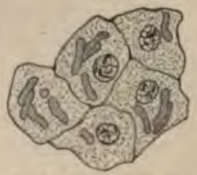

FIG. 609.—Cells of the interstitial tissue of the testis with crystalloid bodies.

is another structure called an *idiosome*, containing a number of microsomes. There are also a coloured or chromatoid body whose function is not known, and two centrosomes (see fig. 608).

The *straight tubules* consist of basement membrane and lining cubical epithelium only.

The interstitial connective tissue of the testis is loose, and contains numerous lymphatic clefts. Lying in it, accompanying the blood-vessels, are strands of polyhedral epithelial cells, of a yellowish colour (*interstitial cells*), which frequently contain crystalloid bodies.

The *tubules of the rete testis* are lined by cubical epithelium; the basement membrane is absent.

The *vasa efferentia, coni vasculosi*, and *epididymis* are lined by columnar cells, some of which are ciliated, whilst others are devoid of cilia, and probably possess secretory functions. There is a good deal of muscular tissue in their walls.

The *vas deferens* consists of a muscular wall (outer layer longitudinal, middle circular, inner longitudinal), lined by a mucous membrane, the inner surface of which is covered by columnar epithelium.

The *vesiculæ seminales* (fig. 606) are outgrowths of the vasa deferentia. Each is a much convoluted, branched, and sacculated tube of structure similar to that of the vas deferens, except that the wall is thinner, and the lining epithelium is often of transitional character.

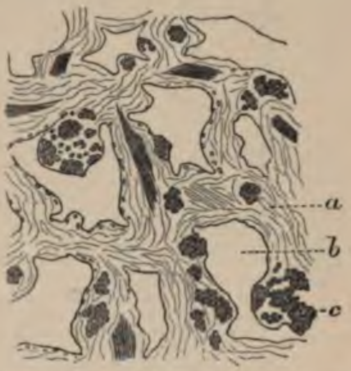

FIG. 610.—Erectile tissue of the human penis. *a*, Fibrous trabeculæ with their ordinary capillaries; *b*, section of the venous sinuses; *c*, muscular tissue. (Cadiat.)

The *penis* is composed of cavernous tissue covered by skin. The cavernous tissue is collected into three tracts, the two *corpora cavernosa* and the *corpus spongiosum* in the middle line inferiorly. All these are enclosed in a capsule of fibrous and plain muscular tissue; the septa which are continued in from this capsule, form the boundaries of the cavernous venous spaces of the tissue. The arteries run in the septa; the capillaries open into the venous spaces. The arteries are often called *helicine*, as in injected specimens they form twisted loops projecting into the cavernous spaces (see also p. 313). The structure of the urethra and prostate is described on pp. 541-543.

The Spermatozoa, suspended in a richly albuminous fluid, constitute the semen. Each spermatozoon consists of a head, a very short neck, a body, a tail, and an end-piece. The head is of flattened ovoid shape, and in the anterior two-thirds of its extent is surmounted by a head-cap which, sharpened at its extremity, forms a cutting edge. The neck is very short, but contains two centrosomes. The body is about the same length as the head; it is traversed by an axial filament and a spiral fibril wound round the sheath of the axial filament. More externally is a layer of punctiform substance called the mitochondrial sheath which terminates at the junction with the tail on an annular disc. The axial filament is continued through the tail into the end-piece, and in the tail is surrounded by thick sheath. In some animals, newts and salamanders, the tail is surrounded by a spiral membrane, but this is not present in the human spermatozoon. The head of the spermatozoon is formed from the nucleus of the spermatid, the head-cap from the idiosome; the centrosomes of the spermatid

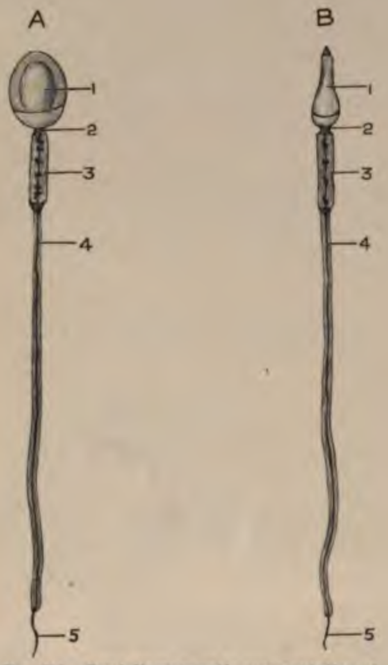

FIG. 611.—Semi-diagrammatic representation of human spermatozoa. A, front view; B, side view. 1, Head cap surrounding head; 2, neck; 3, body; 4, tail; 5, end-piece. The axial filament runs through the body and tail into the end-piece.

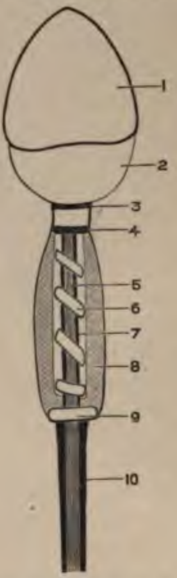

FIG. 612.—Diagram of part of a human spermatozoon highly magnified (after Meves). 1, Head cap; 2, head; 3, anterior centrosome in neck; 4, posterior centrosome in neck; 5, axial filament; 6, spiral sheath; 7, sheath of axial filament in body; 8, mitochondrial sheath; 9, annulus; 10, thick sheath of axial filament in tail.

pass to the neck of the spermatozoon, and the cytoplasm of the spermatid is transformed into the parts of the body and tail of the spermatozoon.

FEMALE ORGANS

The Ovary is a solid organ composed of fibrous tissue (stroma), containing near its attachment to the broad ligament a number of plain muscular fibres. It is covered by a layer of cubical cells, the so-called germinal epithelium, which, in young animals, is seen dipping down, here and there, into the stroma. The stroma contains a number of yellow polyhedral cells similar to the interstitial cells of the testicle.

Sections of the ovary show that the stroma is crowded with a number of rounded cells, the *oocytes*, derived from primitive germ cells, which, in the early stages, were intermingled with the cells of the germinal epithelium. There are also numerous vesicles of different sizes which are called *Graafian follicles.* The smallest follicles are near the surface, the largest are deeply placed, but as they expand they again approach the surface, and ultimately rupture upon it.

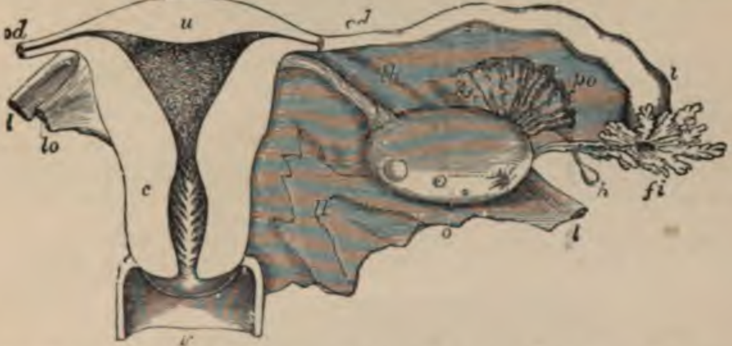

FIG. 613.—Diagrammatic view of the uterus and its appendages, as seen from behind. The uterus and upper part of the vagina have been laid open by removing the posterior wall; the Fallopian tube, round ligament, and ovarian ligament have been cut short, and the broad ligament removed on the left side; *u*, the upper part of the uterus; *c*, the cervix opposite the os internum; the triangular shape of the uterine cavity is shown, and the dilatation of the cervical cavity with the rugæ termed arbor vitæ; *v*, upper part of the vagina; *od*, Fallopian tube or oviduct; the narrow communication of its cavity with that of the cornu of the uterus on each side is seen; *l*, round ligament; *lo*, ligament of the ovary; *o*, ovary; *i*, wide outer part of the right Fallopian tube; *fi*, its fimbriated extremity; *po*, parovarium; *h*, one of the hydatids frequently found connected with the broad ligament. ½. (Allen Thomson.)

A Graafian follicle has an external wall formed by the stroma; this is lined internally by a layer of cells derived from the germinal epithelium which surrounds the oocyte. At a later stage there are two layers of cells, one lining the cavity, and the other surrounding the oocyte, but the two are close together. A viscid fluid collects between the two, and as the follicle grows, separates them.

The cells in each layer multiply, and are eventually arranged in several strata. The lining epithelium of the follicle is then called the *membrana granulosa*, and the heaped mass of cells around the ovum, the *discus proligerus*. The fluid increases in quantity, the follicle becomes tenser, and finally it reaches the surface of the organ and bursts; the ovum is thus set free, and is seized by the fringed

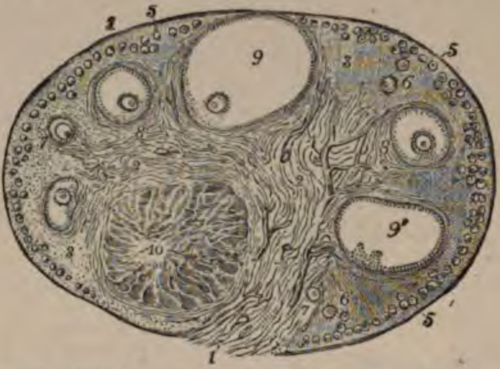

FIG. 614.—View of a section of the ovary of the cat. 1, Outer covering and free border of the ovary; 1', attached border; 2, the ovarian stroma, presenting a fibrous and vascular structure; 3, granular substance lying external to the fibrous stroma; 4, blood-vessels; 5, ovigerms in their earliest stages occupying a part of the granular layer near the surface; 6, ovigerms which have begun to enlarge and to pass more deeply into the ovary; 7, ovigerms round which the Graafian follicle and tunica granulosa are now formed, and which have passed somewhat deeper into the ovary and are surrounded by the fibrous stroma; 8, more advanced Graafian follicle with the ovum imbedded in the layer of cells constituting the proligerous disc; 9, the most advanced follicle containing the ovum, etc.; 9', a follicle from which the ovum has accidentally escaped; 10, corpus luteum. (Schrön.)

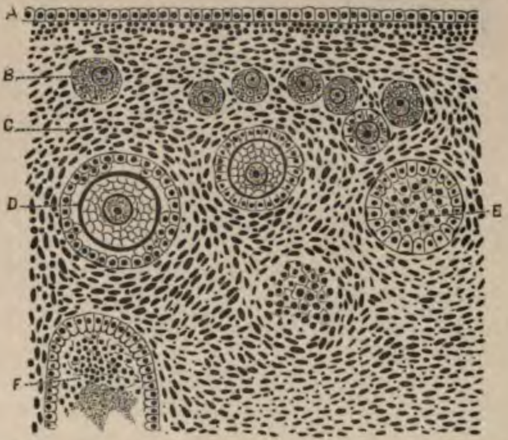

FIG. 615.—Section of the ovary of a cat. A, germinal epithelium; B, immature Graafian follicle; C, stroma of ovary; D, vitelline membrane containing the ovum; E, Graafian follicle showing lining cells; F, follicle from which the ovum has fallen out. (V. D. Harris.)

ends of the Fallopian tube and thence passes to the uterus. The bursting of a Graafian follicle usually occurs about the time of menstruation.

After the bursting of a Graafian follicle, it is filled up with what is known as a *corpus luteum.* This is derived from the wall of the follicle, and consists of columns of yellow cells developed from the yellow cells of the membrana granulosa; it contains a blood-clot in its centre. These cells multiply, and their strands get folded and converge to a central strand of connective tissue; between the columns there are septa of connective tissue with blood-vessels. The corpus luteum after a time gradually disappears; but if pregnancy supervenes it becomes larger and more persistent (see fig. 616). The following table gives the chief facts in the life-history of the ordinary corpus luteum of menstruation, compared with that of pregnancy:—

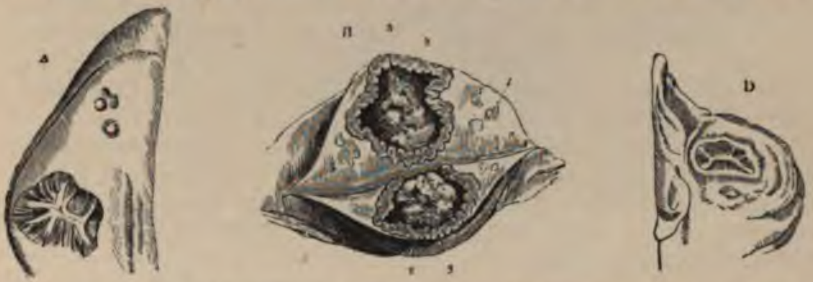

FIG. 616.—Corpora lutea of different periods. B, Corpus luteum of about the sixth week after impregnation, showing its plicated form at that period. 1, Substance of the ovary; 2, substance of the corpus luteum; 3, a greyish coagulum in its cavity. (Paterson.) A, Corpus luteum two days after delivery; D, in the twelfth week after delivery. (Montgomery.)

	Corpus Luteum of Menstruation.	**Corpus Luteum of Pregnancy.**
At the end of three weeks.	Three-quarters of an inch in diameter; central clot reddish; convoluted wall pale.	
One month .	Smaller; convoluted wall bright yellow; clot still reddish.	Larger; convoluted wall bright yellow; clot still reddish.
Two months .	Reduced to the condition of an insignificant cicatrix.	Seven-eighths of an inch in diameter; convoluted wall bright yellow; clot perfectly decolorised.
Six months .	Absent.	Still as large as at end of second month; clot fibrinous; convoluted wall paler.
Nine months .		One half an inch in diameter; central clot converted into a radiating cicatrix; the external wall tolerably thick and convoluted, but without any bright yellow colour.

It has been suggested that the corpus luteum yields an internal secretion, the effect of which is to assist gestation in some at present unknown way.

Many of the Graafian follicles never burst; they attain a certain degree of maturity even during childhood, then atrophy and disappear.

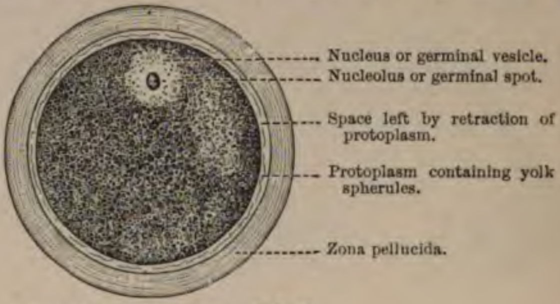
Nucleus or germinal vesicle.
Nucleolus or germinal spot.
Space left by retraction of protoplasm.
Protoplasm containing yolk spherules.
Zona pellucida.

FIG. 617.—A human ovum. (Cadiat.)

The ovarian ovum or oocyte of the first order (fig. 617) is a large spheroidal cell surrounded by a transparent striated membrane called the *zona pellucida*, or *zona striata*. The protoplasm is filled with large

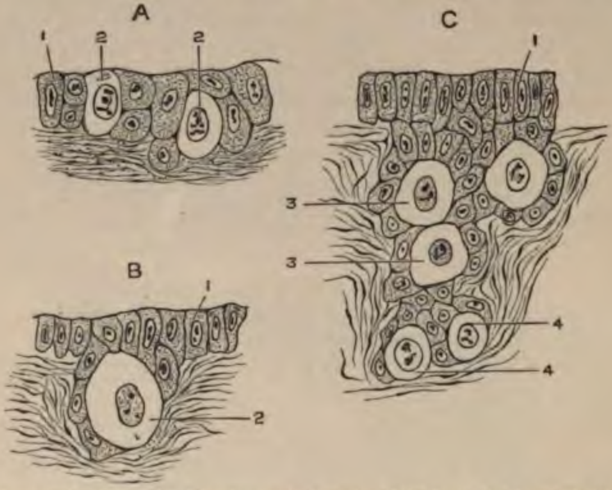

FIG. 618.—Diagram showing mode of development of oocytes of the first order from primitive germ cells in mammalian ovary. 1, germinal epithelium; 2, primitive germ cells; 3, oogonia; 4, oocytes of the first order. In A, two primitive germ cells are seen imbedded in the germinal epithelium. In B, a primitive germ cell has descended into the stroma of the ovary accompanied by cells proliferated from the germinal epithelium which will become the cells of the membrana granulosa. In C, the oogonia derived from primitive germ cells, and oocytes of the first order produced by division of the oogonia, are seen. (After Bühler.)

fatty and albuminous granules (*yolk spherules*), except in the part around the nucleus, which is comparatively free from these granules. It contains a nucleus which has the usual structure of nuclei; there is generally one very well-marked nucleolus. The nucleus and nucleolus are still often called by their old names, *germinal vesicle* and *germinal spot* respectively. An attraction sphere, not shown in the figure, is also present, and a fine membrane, the *vitelline membrane*, is said to lie between the protoplasm and the zona pellucida.

The oocytes are developed from the primitive germ cells which in the earliest stages are interspersed between the cells of the germinal epithelium. The primitive germ cells divide and produce *oogonia;* and by the division of the oogonia, oocytes are formed (fig. 618). As the oogonia and oocytes are developed they sink into the stroma, surrounded by cells, produced by the proliferation of the germinal epithelium, which are destined to form the membrana granulosa and the discus proligerus.

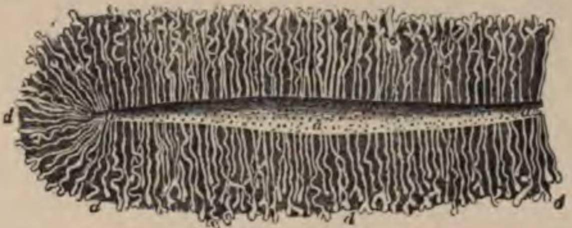

FIG. 619.—Section of the lining membrane of a human uterus at the period of commencing pregnancy, showing the arrangement of the glands, *d*, *d*, *d*, with their orifices, *a*, *a*, *a*, on the internal surface of the organ. Twice the natural size.

The Fallopian tubes have externally a serous coat derived from the peritoneum, then a muscular coat (longitudinal fibres outside, circular inside), and most internally a very vascular mucous membrane thrown into longitudinal folds, and covered with ciliated epithelium.

The uterus consists of the same three layers. The muscular coat is, however, very thick and is made up of two strata imperfectly separated by connective tissue and blood-vessels. Of these the thinner outer division is the true muscular coat, the fibres of which are arranged partly longitudinally, partly circularly. The inner division is very thick; its fibres run chiefly in a circular direction; the extremities of the uterine glands extend into its internal surface. It is in fact a much hypertrophied muscularis mucosæ.

The mucous membrane is thick, and consists of a corium of soft connective tissue, lined with ciliated epithelium; this is continued down into long tubular glands which have, as a rule, a convoluted course. In the cervix the glands are shorter. Near the os uteri the epithelium becomes stratified; stratified epithelium also lines the vagina.

At each menstrual period the uterus becomes congested, and some of the blood-vessels of the mucous membrane are ruptured; the blood, together with the secretion of the glands and some epithelial *débris* from the surface, constitutes the menstrual flow, which usually lasts two or three days. The amount of destruction of the surface epithelium is not, however, a marked phenomenon; still less is there any disintegration of the deeper parts of the mucous membrane.

For Parturition (see p. 677), and for a description of the mammary glands (see p. 464).

CHAPTER LIX

DEVELOPMENT

The description of the origin and formation of the tissues and organs constitutes the portion of biological science known as embryology. All one can possibly attempt in a physiological text-book is the merest outline of the principal facts of development.

In our descriptions we shall speak principally of the development of the mammal; it will not be possible to do so altogether, for many of the facts which are believed to be true of the mammal (man included) have only been actually seen in the lower animals. That they occur in the higher animals is a matter of inference.

It will, however, add interest to the subject to draw some of our descriptions from the lower animals; for the scientific discussion of embryology must always start from a wide survey of the whole animal kingdom, because the changes which occur in the embryological history of the highest animals, form a compressed picture of the changes which have taken place in their historical development from lower types.

The Ovum.

The human ovum is like that of other mammals, a small cell about $\frac{1}{125}$ to $\frac{1}{150}$ inch in diameter.

The changes by which the ovum, or a portion of the ovum, is transformed into the young animal may take place either inside or outside the body of the parent. If they take place inside the parent, as in mammals, including the human subject, the ovum is small, and the nutriment necessary for its growth and development is derived from the surrounding tissues and fluids of the mother. If the development takes place outside the parent's body, as in birds, the egg is larger; it contains a large amount of nutritive material called the yolk, and it may, in addition, be surrounded by sheaths of nutritive substance. Thus, in the hen's egg, the yellow part alone is comparable with the mammalian ovum, and the larger part of that is merely nutritive substance; upon it is a whitish speck, the cicatricula, about $\frac{1}{8}$ of an inch in diameter. In the cicatricula lies the nucleus or germinal vesicle, and it is this small mass of protoplasmic substance which divides and grows to produce the chick; the yolk and the surrounding white being used as food.

Ova like the hen's, in which only a small part, the cicatricula, divides and grows, are called meroblastic. Small ova, with little food yolk, such as the human ovum, divide completely during development, and are called holoblastic, but numerous gradations occur between the two extreme types.

The structure of the mammalian ovum and its mode of formation have already been considered (p. 824), but before such an ovum can develop it must first become mature, and then it must be impregnated by the entrance of a spermatozoon.

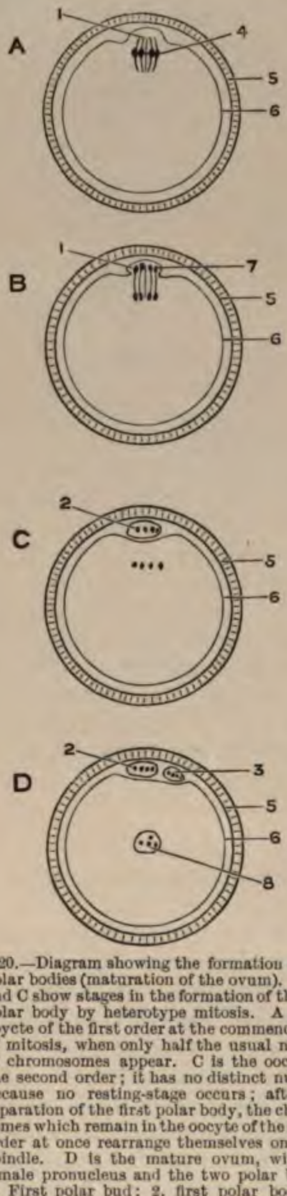

FIG. 620.—Diagram showing the formation of the polar bodies (maturation of the ovum). A, B, and C show stages in the formation of the first polar body by heterotype mitosis. A is the ooycte of the first order at the commencement of mitosis, when only half the usual number of chromosomes appear. C is the oocyte of the second order; it has no distinct nucleus, because no resting-stage occurs; after the separation of the first polar body, the chromosomes which remain in the oocyte of the second order at once rearrange themselves on a new spindle. D is the mature ovum, with the female pronucleus and the two polar bodies. 1, First polar bud; 2, first polar body; 3, second polar body; 4, chromosomes on spindle of oocyte of first order; 5, zona striata; 6, vitelline membrane; 7, daughter chromosomes in first polar bud; 8, female pronucleus.

Maturation of the Ovum.

It will be remembered that the germ cells which form the ova are at first embedded in the germinal epithelium, from which they pass into the stroma of the ovary, and then by division and growth they form oogonia; from the oogonia, oocytes of the first order are developed, and the oocytes of the first order become enclosed in Graafian follicles. It is the process by which the oocytes of the first order become converted into mature ova, which is known as maturation, and it consists essentially of a double mitotic division of the oocyte, each division producing two unequal parts. The first division produces an oocyte of the second order and the first polar body, and the second, which takes place without any resting-stage, results in the formation of the mature ovum and the second polar body. Thus, when the two divisions are completed, the mature ovum and two polar bodies lie inside the zona pellucida. In some cases, only one polar body is formed, that is, only one division occurs.

The unequal division is naturally associated with an eccentric position of the spindle. At each division one end of the spindle projects in the surface with a little surrounding protoplasm, and it is the small process which becomes the polar body.

One of the essential features of maturation is the reduction of the number of chromosomes in the nucleus. It is well known that the nuclei of all animal cells, including germ cells and oogonia, contain a definite number of chromatic particles. When maturation commences in the oocytes of the first order, an achromatic spindle is formed in the usual way; but instead of the ordinary number of chromosomes appearing at its equator, only half that number are seen: for example, if eight be the normal number of chromosomes, only four appear. Further, each chromosome is not a slender V-shaped loop, but a short, thick rod, or ring, or group of four particles. Neither does it split longitudinally in the usual way, but transversely; and at the end of the process the oocyte of the second order and the first polar body both contain four chromosomes. This form of mitosis is known as heterotype, whilst the ordinary form is called homotype. The second division which produces the mature ovum and the second polar body is of the homotype form, and the final result is that each of the segments into which the oocyte of the first order has divided

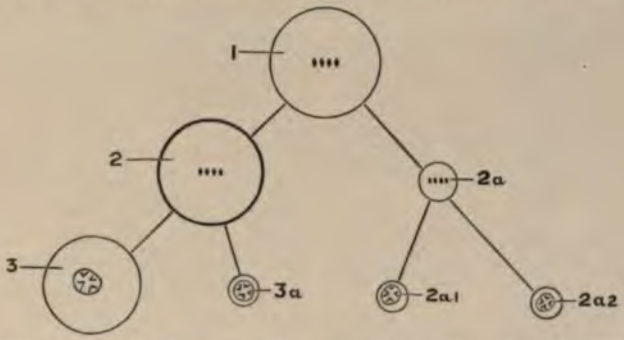

FIG. 621.—Diagram showing the stages in the maturation of the ovum when the first polar body divides. A similar diagram would represent the formation of spermatids from a spermatocyst of the first order. 1, Oocyte of the first order; 2, oocyte of the second order; 2*a*, first polar body; 3, mature ovum; 3*a*, second polar body; 2*a*1, and 2*a*2, daughter cells of the first polar body. All the last generation in the male would be spermatids of equal value.

—the mature ovum and the two polar bodies—contains half the number of chromosomes present in the parent germinal cell. In some cases the first polar body divides at the same time that the second polar body is formed, and the process may be represented by the schema in fig. 621.

The nucleus of the mature ovum is known as the female pronucleus.

Impregnation.

By impregnation is meant the union of a spermatozoon with an ovum. The spermatozoon, moving by the flagellar movement of its tail meets the mature ovum in the upper part of the Fallopian tube, and by means of its sharp head cap it pierces the zona pellucida, and the head, neck, and possibly part of the body, enter the substance of the ovum, where they undergo transformation, and are converted into a male pronucleus with an attendant attraction sphere and its centrosome. The male pronucleus contains the same number of chromosomes as the female pronucleus, for the mitosis which occur when the spermatocyst of the first order divides to form the two spermatocysts of the second order, is a heterotype mitosis, in which only half the usual number of chromosomes appear; and consequently the spermatocysts of the second order, and their descendants the spermatids, also contain only half the typical number of chromosomes. These are retained in the spermatozoa, which are produced by modification of the spermatid, and they reappear in the male pronucleus.

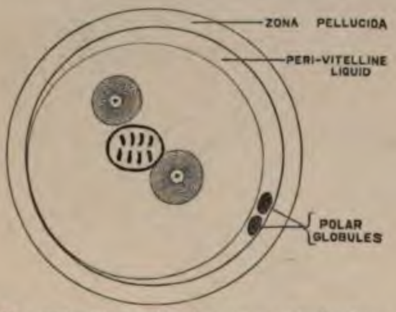

Fig. 622.—The fertilised ovum or blastosphere, showing its new nucleus and attraction spheres; the yolk granules have been omitted.

After the male pronucleus has formed in the substance of the mature ovum, it approaches the female pronucleus, and when the two pronuclei fuse, fertilisation is completed. The nucleus which results from the fusion—the first segmentation nucleus—contains the typical number of chromosomes, half being derived from the female and half from the male germinal element. When the fertilisation is completed, the segmentation nucleus is accompanied by two attraction spheres with their centrosomes (see fig. 622); one of these spheres is that associated with the male pronucleus, but the origin of the other is uncertain. It may belong to the ovum, though it was not apparent during the maturation, or it may have been produced by the division of the centrosome and attraction sphere which accompany the male pronucleus.

Segmentation.

After fertilisation is completed, the ovum divides into two parts; each of these again divides, and so on till a mulberry-shaped mass—the morula—is formed. It consists of a large number of small cells, and it is enclosed together with the polar bodies, in the zona pellucida. The polar bodies soon disappear; indeed in many cases they have vanished long before the morula is completed. A cavity soon appears in the morula, which thus becomes converted into a blastula or blastocyst. The cells which form the peripheral wall of the blastula assume a more or less cubical form, whilst those which lie in the interior and form the inner cell mass are irregular in outline, and they are grouped together at one pole of the blastula. At this period the blastula is unilaminar, except at the region where the inner cell mass is situated; but soon the cells of the inner mass extend round the cavity and the wall of the cyst becomes bilaminar. In amphioxus and in many invertebrates the blastula is at first entirely unilaminar, no inner cell mass being present. In these cases the inner layer is formed by the invagination of a part of the wall of the vesicle, and the opening at which the invagination occurs is known as the blastopore or primitive mouth.

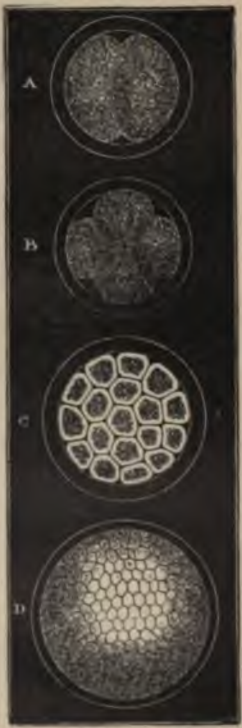

FIG. 623.—Diagrams of the various stages of cleavage of the ovum. (Dalton.)

If the surface of a bilaminar mammalian blastoderm is examined, an area is found which is darker or more opaque than the rest; this is the area where the embryo will be formed, and it is known as the germinal or embryonic area (fig. 624). It corresponds with the region where the inner mass is adherent to the outer layer, and in it the epiblast cells are of cubical or columnar form, whilst over the remainder of the wall of the vesicle they have been transformed into flattened plates (fig. 625). At first the germinal area is circular, then it becomes ovoid, and ultimately pear-shaped, the narrow part of the pear-shaped area indicating the region of the posterior end of the body of the future embryo (fig. 626). A linear streak—the primitive streak—quickly appears in the narrow part of the area, and after a time, a groove—the primitive groove—appears on its surface. In the meantime, a second groove has appeared on the surface of the ovum in front of the primitive streak. This is the neural groove or rudiment of the central canal of the brain and spinal cord. It is bounded by two folds—the neural folds, which are united together at their anterior ends, but their posterior ends which embrace the anterior end of the primitive streak do not unite until after the appearance of the opening at the anterior end of the primitive streak. This opening therefore connects the neural groove with the cavity in the interior of the blastodermic vesicle, which is called the archenteric cavity, and through it the epiblast becomes continuous with the hypoblast. Therefore it evidently represents a part of the blastopore of more primitive forms, but it is called the neurenteric canal. It soon closes, and all traces of it are lost.

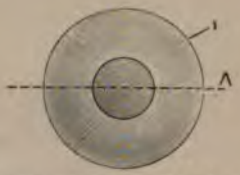

FIG. 624.—Diagram of a surface view of a young mammalian blastula. 1, Germinal area. A, line of section represented in fig. 625.

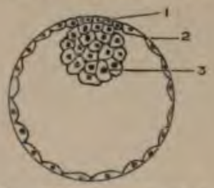

FIG. 625.—Diagram of a section of the mammalian blastula shown in fig. 624 along the line A. 1, Germinal area; 2, epiblast; 3, inner cell mass.

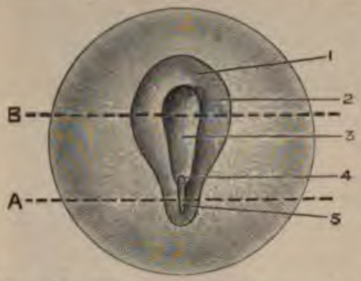

FIG. 626.—Diagram of a surface view of a mammalian blastoderm after the formation of the neural groove. 1, Germinal area; 2, neural ridge; 3, neural groove; 4, neurenteric canal (part of blastopore); 5, primitive groove and streak. A, line of section shown in fig. 627; B, line of section shown in fig 628.

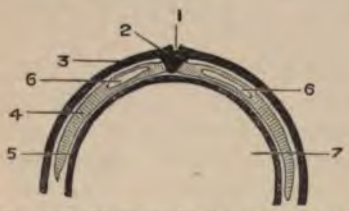

FIG. 627.—Diagram of a transverse section through a mammalian blastoderm along line A in fig. 626. 1, primitive groove; 2, primitive streak; 3, epiblast; 4, mesoblast; 5, hypoblast; 6, cœlom; 7, archenteron.

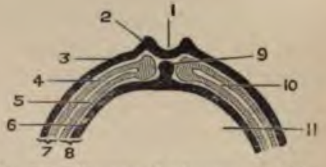

FIG. 628.—Diagram of a transverse section through a mammalian blastoderm along line B in fig. 626. 1, neural groove; 2, neural ridge; 3, epiblast; 4, somatic mesoblast; 5, splanchnic mesoblast; 6, hypoblast; 7, somatopleur: 8, splanchnopleur; 9, notochord; 10, cœlom; 11, archenteron.

The primitive streak itself is due to a down-growth of a linear ridge of epiblastic cells, and soon after its formation a layer of cells, the mesoblast, or third layer of the blastoderm, grows out from its sides and posterior end, and extends between the epiblast and hypoblast over the whole area of the vesicle.

That portion of the mesoblast which lies immediately at the sides of the neural groove becomes partially separated from the rest, and at the same time divided into cuboidal blocks, the protovertebræ or mesoblastic somites. The more laterally situated part of the mesoblast constitutes the lateral plates, and the narrow strand of mesoblastic cells which connects the lateral plate on each side with the protovertebral somites is the intermediate cell mass. Soon after its formation the lateral mesoblast is cleft into two layers, and the space which appears between the two layers is called the cœlom (figs. 627, 628). The outer or somatic layer of the mesoblast adheres to the epiblast; the two together form the somatopleur. The inner or splanchnic layer fuses with the hypoblast to form the splanchnopleur. Cavities also appear in the mesoblastic somites.

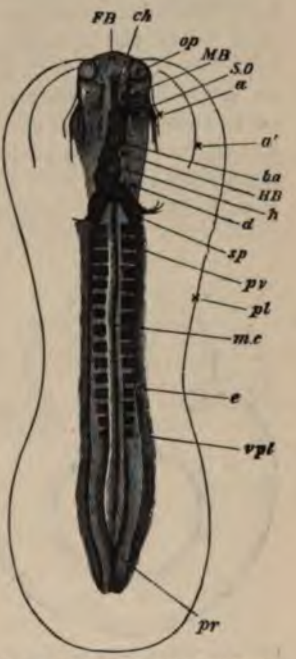

FIG. 629.—Embryo chick (36 hours), viewed from beneath as a transparent object (magnified). *pl*, Outline of pellucid area; *FB*, fore-brain, or first cerebral vesicle: from its sides project *op*, the optic vesicles; *SO*, backward limit of somatopleur fold, "tucked in" under head; *a*, head-fold of true amnion; *a'*, reflected layer of amnion, sometimes termed "false amnion"; *sp*, backward limit of splanchnopleur folds, along which run the omphalo-mesenteric veins uniting to form *h*, the heart, which is continued forwards into *ba*, the bulbus arteriosus; *d*, the fore-gut, lying behind the heart, and having a wide crescentic opening between the splanchnopleur folds; *HB*, hind-brain; *MB*, mid-brain; *pv*, protovertebræ lying behind the fore-gut; *mc*, line of junction of medullary folds and of notochord; *ch*, front end of notochord; *vpl*, vertebral plates; *pr*, the primitive groove at its caudal end. (Foster and Balfour.)

Whilst the mesoblast is extending and cleaving, the neural folds gradually grow in height, and their free margins turn inwards and fuse together. This fusion commences in the cervical region, and extends forwards and backwards, and when it is completed the neural groove is converted into a closed tube, the neural tube, and the original groove is now the central canal of the nervous system. In the ovum at this period there are, therefore, three cavities: (1) The neural or central canal confined to the embryonic region; (2) The cœlom or space in the mesoblast; (3) The archenteron within the hypoblast. The embryonic area is still outspread on the surface of the ovum. When the changes to which reference has been made are well advanced, and in many cases before the neural groove is closed, the embryonic area begins to fold off from the rest of the ovum. A sulcus appears all round the margins of the area, and over this sulcus the area bends forwards, backwards, and laterally. It looks as if some constricting agent had been placed round the margin of the area, and that afterwards the area above the constriction, and the area below had gone on growing rapidly. In this way, the ovum is clearly separated into two parts, an upper, the embryo, and a lower, which becomes the appendages of the embryo. The anterior part of the folded embryonic area is known as the head fold, the posterior as the tail fold, and the two are connected together on each side by the lateral folds. As the constriction between the embryonic and non-embryonic parts affects the interior as well as the exterior of the ovum, it follows that three cavities are present in the embryo. (1) The central canal of the neural tube, which is of course lined by epiblast. (2) A portion of the archenteron lined by hypoblast. (3) A portion of the cœlom or cavity of the mesoblast (fig. 630).

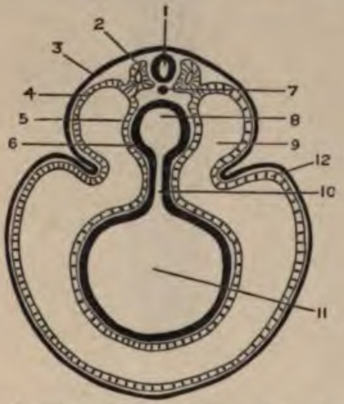

FIG. 630.—Diagram of a transverse section through a mammalian ovum at the period when the folding off of the embryo has commenced. 1, Neural tube; 2, protovertebral somite; 3, epiblast; 4, somatic mesoblast; 5, splanchnic mesoblast; 6, hypoblast; 7, notochord; 8, primitive alimentary canal; 9, cœlom; 10, vitello-intestinal duct; 11, yolk sac; 12, lateral fold of amnion.

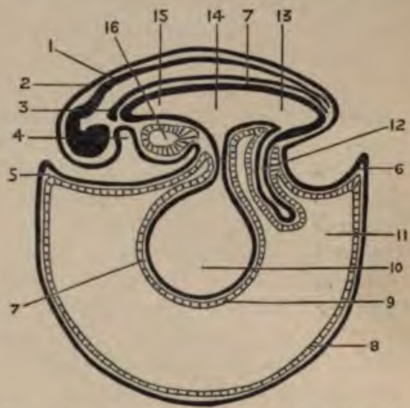

FIG. 631.—Diagram of a longitudinal section of a mammalian ovum at the period when the folding off of the embryo has commenced. 1, Neural tube; 2, epiblast; 3, notochord; 4, stomadœal space; 5, head fold of amnion; 6, tail fold of amnion; 7, hypoblast; 8, somatic mesoblast; 9, splanchnic mesoblast; 10, yolk sac; 11, cœlom; 12, allantois; 13, hind-gut; 14, mid-gut; 15, fore-gut; 16, pericardium.

The central canal of the neural tube, as before stated, becomes the cavity of the permanent central nervous system, and it forms the central canal of the spinal cord, the lateral, third and fourth ventricles, and the aqueduct of Sylvius which connects the third and fourth ventricles together.

The portion of the archenteron enclosed in the embryo forms the primitive gut. The part contained in the head fold is the fore-gut, that in the tail fold is the hind-gut, and the remainder is the mid-gut (fig. 631).

The constriction where the body of the embryo becomes continuous with the remainder of the ovum, is known ultimately as the umbilicus. It remains pervious till birth, when the embryo is separated from the rest of the ovum, and through it the mid-gut is connected with the remainder of the archenteron (which is henceforth called the yolk sac) by a narrow hypoblastic tube, the vitello-intestinal duct (fig. 630, 10).

The portion of the mesoblastic cavity enclosed in the embryo is called the body cavity. It gradually differentiates into the pericardial pleural and peritoneal cavities, which are eventually entirely separated from each other.

In the early stages the gut is close to the posterior wall of the body, but after a time it advances into the body cavity; it remains connected, however, with the dorsal wall by a fold of the splanchnic portion of the mesoblast, which is called the dorsal mesentery. A similar mesentery is found connecting the ventral wall of that portion, fore-gut, which becomes stomach and duodenum, with the ventral wall of the body.

Before the neural groove is closed and becomes the neural canal, the hypoblast beneath the middle of the groove becomes thickened to form a longitudinal ridge (fig. 628). This ridge is the notochord or primitive skeletal axis. It soon separates from the remainder of the hypoblast, and forms a round cord, which lies at first immediately beneath the neural groove, and afterwards beneath the neural tube, extending from the anterior end of the primitive gut, which lies beneath that region of the neural tube which afterwards becomes the mid-brain, to the caudal end of the embryo (figs. 630, 631).

It follows from what has already been stated, that the embryo attains its distinct form by a process of folding; but for some time after it is separated off from the remainder of the ovum (except at the margins of the umbilical orifice), it has no limbs. After a time a ridge appears on each side of the body, along the line of the intermediate cell mass in the interior; this is the Wolffian ridge, and from its anterior and posterior parts, the limbs grow out as small horizontal ledges.

The differentiated embryo contains parts of all the layers of the blastoderm, and from each of these certain organs are formed as indicated in the following list.

1. **From Epiblast.**—*a.* The epidermis and its appendages.
b. The nervous system, both central and peripheral.
c. The epithelial structures of the sense-organs.
d. The epithelium of the mouth, the enamel of the teeth.

e. The epithelium of the nasal passages.

f. The epithelium of the glands opening on the skin and into the mouth, and nasal passages.

g. The muscular fibres of the sweat-glands.

2. **From Mesoblast.**—*a.* The skeleton and all the connective tissues of the body.

b. All the muscles of the body.

c. The vascular system, including the lymphatics, serous membranes, and spleen.

d. The urinary and generative organs, except the epithelium of the bladder and urethra.

The Somatic mesoblast forms the osseous, fibrous, and muscular tissues of the body-wall, including the true skin.

The Splanchnic mesoblast forms the fibrous and muscular wall of the alimentary canal, the vascular system, and the urino-genital organs.

3. **From Hypoblast.**—*a.* The epithelium of the alimentary canal from the back of the mouth to the anus, and that of all the glands (including liver and pancreas) which open into this part of the alimentary tube.

b. The epithelium of the respiratory cavity.

c. The epithelium of the Eustachian tube and tympanum.

d. The epithelium lining the vesicles of the thyroid.

e. The epithelial nests of the thymus.

f. The epithelium of the bladder and urethra.

The Decidua and the Fœtal Membranes.

When the uterus is ready for the reception of an ovum it is lined by a greatly hypertrophied mucous membrane, called the decidua, because, after the delivery of the child, a portion of it comes away from the uterus with the other membranes.

When the ovum, which has been fertilised in the upper part of the Fallopian tube, reaches the uterine cavity, it is usually in the stage of a morula or blastula. It rapidly eats its way into the substance of the decidua which closes over it, obliterating the opening through which it passed, and thus the ovum becomes embedded in the membrane, which thereupon becomes separable into three parts. 1. The part between the ovum and the muscular wall of the uterus, the *decidua basalis.* 2. The part between the ovum and the uterine cavity, the *decidua capsularis or reflexa.* 3. The remaining part is called the *decidua vera.* Between the decidua capsularis and the decidua basalis lies the ovum, which speedily becomes differentiated into embryo, membranes, and appendages. The outermost of the fœtal membranes is the chorion; this is covered with vascular villi, which dip into the decidua capsularis and basalis. Inside the chorion is the amnion, a closed sac, which surrounds the embryo and is attached to its ventral wall at the umbilicus. The amnion also forms a sheath for the umbilical cord by which the embryo is attached to the inner surface of the chorion; it is filled with fluid, the amniotic fluid, in which the fœtus floats; the umbilical cord contains not only the blood-vessels which pass between a specialised portion of the chorion, which forms the fœtal part of the placenta, and the embryo, but also the remains of the yolk-sac, and the duct by which it is connected with the intestine of the embryo.

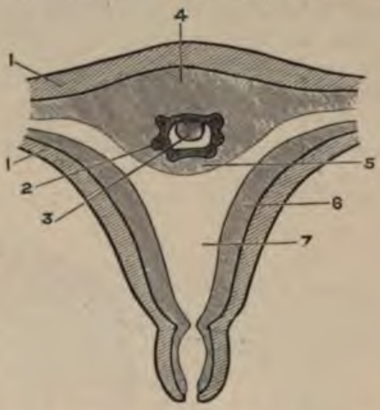

FIG. 632.—Diagram representing the relation of the developing ovum to the decidua at a very early stage. 1, Uterine muscle; 2, epiblast of ovum; 3, inner cell mass of ovum (hypoblast); 4, decidua basalis; 5, decidua capsularis; 6, decidua vera; 7, cavity of uterus.

As the ovum grows, the decidua capsularis is expanded over its surface, and as the growth continues the uterine cavity is gradually obliterated, and the decidua capsularis is forced into contact with the decidua vera, with which it fuses.

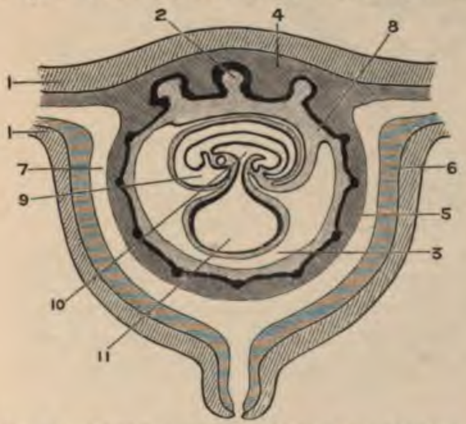

FIG. 633.—Diagram representing a later stage of development than that shown in fig. 632. 1, Uterine muscle; 2, villi of chorion of ovum; 3, cœlom; 4, decidua basalis; 5, decidua capsularis; 6, decidua vera; 7, cavity of uterus; 8, allantois; 9, amnion cavity; 10, primitive intestine; 11, yolk-sac.

As the decidua is merely thickened mucous membrane, it naturally contains glands which become enlarged as the decidua thickens. It was believed, at one time, that the villi of the chorion entered the glands, but this is now known to be incorrect. The villi enter the interglandular substance, and, in the human subject, the glands of the decidua capsularis eventually disappear entirely. In the decidua basalis and the decidua vera the superficial portions of the glands also disappear; their deep portions remain in an almost unchanged condition, and furnish the epithelium for the regeneration of the glands and the lining of the uterine cavity after parturition. The intermediate parts of the glands in the decidua vera and the decidua basalis become very much enlarged, and form a stratum of the decidua called the spongy layer, and ultimately this layer is converted into a series of clefts, and it is along the line of these clefts that the decidua is separated at birth.

In some mammals in which the connection between the chorion and the decidua is less intimate than in the human subject, the glands persist to a greater or less extent, and secrete a fluid called uterine milk, which is absorbed by the chorion.

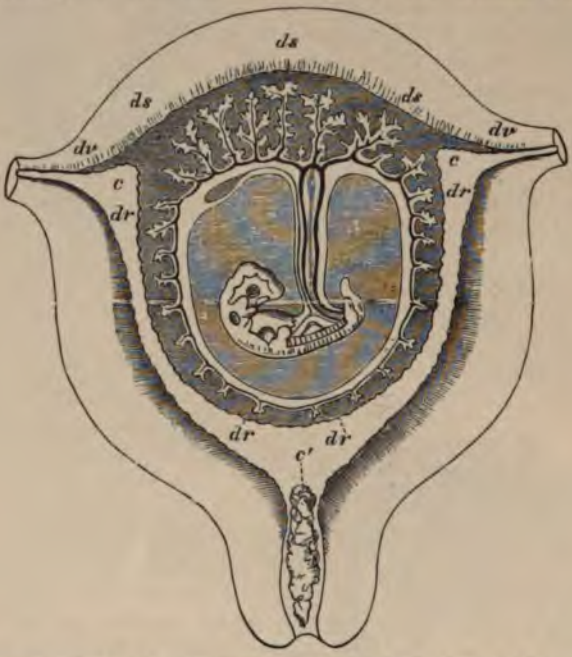

FIG. 634.—Diagrammatic view of a vertical transverse section of the uterus at the seventh or eighth week of pregnancy. *c, c, c'*, cavity of uterus, which becomes the cavity of the decidua, opening at *c, c*, the cornua, into the Fallopian tubes, and at *c'* into the cavity of the cervix, which is closed by a plug of mucus; *dv*, decidua vera; *dr*, decidua reflexa, with the sparser villi embedded in its substance; *ds*, decidua basalis or serotina, involving the more developed chorionic villi of the commencing placenta. The fœtus is seen lying in the amniotic sac; passing up from the umbilicus is seen the umbilical cord and its vessels passing to their distribution in the villi of the chorion; also the pedicle of the yolk-sac, which lies in the cavity between the amnion and chorion. (Allen Thomson.)

The portion of the decidua which undergoes the greatest change is the decidua basalis, formerly called the decidua serotina. In it a number of large blood spaces are formed, and these are separated into masses or cotyledons by fibrous strands. The cotyledons are penetrated by chorionic villi, and it is this conjunction of chorionic villi and decidua basalis which produces the placenta, which, at full term, is seven or eight inches across, and weighs nearly a pound.

The placenta is the organ of fœtal nutrition and excretion. Its blood sinuses are filled with maternal blood, which is carried to them by the uterine arteries and away from them by the uterine veins. Into these blood-filled spaces the vascular fœtal villi project; hence it is easy for exchanges to take place between the fœtal and the maternal blood, though the two blood-streams never mix together. Oxygen and nutriment pass from the maternal blood through the coverings of the fœtal vessels into the fœtal blood, and carbonic acid, urea, and other waste products pass in the contrary direction. The fœtal blood is carried to the placenta by the umbilical arteries, which are the terminal branches of the aorta of the fœtus; these pass to the placenta by the umbilical cord, and the blood is returned, through the cord, by the umbilical vein.

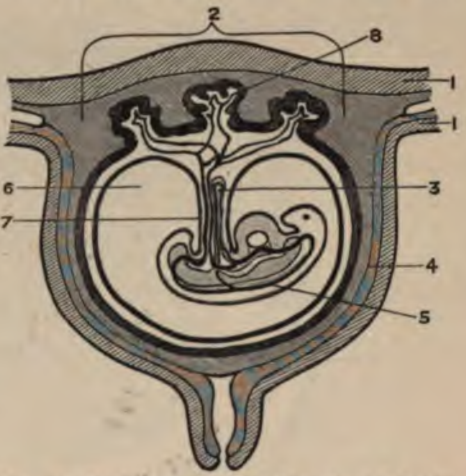

FIG. 685.—Diagram representing a later stage of development of membranes and placenta than that shown in fig. 683. 1, Uterine muscle; 2, placenta; 3, yolk-sac; 4, fused decidua vera and capsularis; 5, primitive blood-vessel of embryo; 6, amnion cavity (outer surface of amnion is fused with inner surface of chorion); 7, umbilical cord; 8, fœtal villus in placenta. For blood-vessels see subsequent figures.

Development of the Fœtal Appendages and Membranes.

The manner in which the primitive intestinal canal is separated from the yolk-sac during the folding off of the embryo from the ovum, has already been considered (p. 834).

In birds the yolk-sac affords nutriment till the end of incubation, and the omphalo-mesenteric blood-vessels which convey the nutriment to the embryo, are correspondingly well developed. In mammalia, the office of the umbilical vesicle ceases at an early period, for the quantity of yolk is small, and the embryo soon becomes independent of it, on account of the intimate relations established with the maternal blood in the placenta. In birds, moreover, as the yolk-sac empties, it is gradually withdrawn into the abdomen of the chick through the umbilical opening which then closes over it. In mammals it remains outside the embryo, and in man its remnants, in a contracted and shrivelled condition, are found in the umbilical cord. In some mammals, however, it plays a much more important part than it does in man, and the time and mode of its disappearance differ in different orders of mammals.

At an early stage, and whilst the changes to which reference has been made are proceeding, three important structures, the amnion, the chorion, and the allantois, are developed.

Amnion.—As the embryo is differentiated, the surface of the ovum beyond its margins, formed by somatopleur, is gradually raised as a circular fold which is looked upon as consisting of head, tail, and lateral portions. The various parts of the fold rise quickly and converge over the embryo, which, at the same time, passes towards the interior of the ovum. Finally the folds meet and fuse together at a point which is called the amnion navel. As soon as the folds fuse, the inner parts separate from the outer and form a closed sac (figs. 630 to 639). The inner wall of the sac is formed by epiblast, the outer by mesoblast, and both are continuous with the same layers of the embryo at the umbilical orifice. At first the amnion closely invests the embryo, but soon the space between the two, the *amniotic cavity*, becomes filled with fluid, and this increases in amount, till at the end of pregnancy it is present in very considerable quantity.

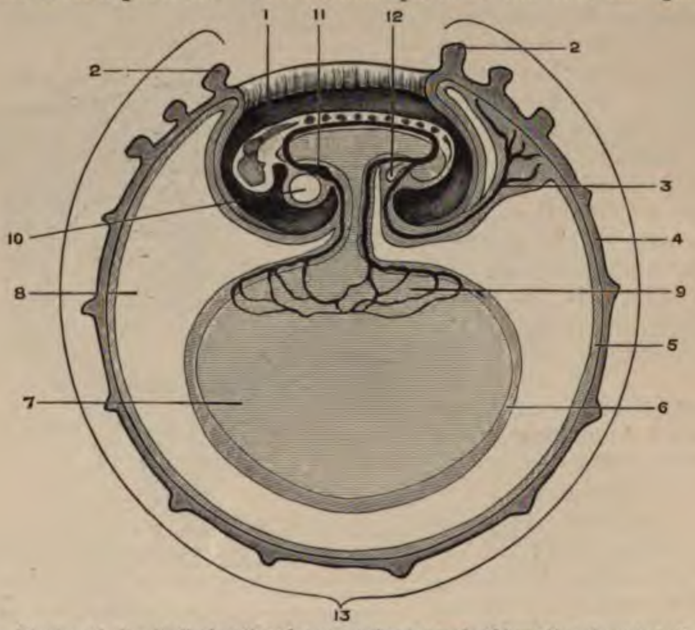

FIG. 636.—Diagram of a longitudinal section of an ovum showing mode of formation of amnion, allantois, and the primitive blood-vessels. 1, Amnion cavity; 2, villi on placental part of chorion; 3, allantois; 4, epiblast of chorion; 5, somatic mesoblast; 6, splanchnic mesoblast; 7, yolk-sac; 8, cœlom; 9, vascular area on yolk-sac; 10, pericardium; 11, heart; 12, allantois diverticulum from cloaca; 13, chorion.

The *amniotic fluid* consists of water containing small quantities of albumin, urea, and salts. It is an exudation from the fœtal and the maternal blood, and the urea in it comes from the fœtal urine which is passed into the amniotic cavity in the later part of pregnancy.

The function of the fluid appears to be purely mechanical. It supports the embryo on all sides, and protects it from blows and other injuries to the abdomen of the mother, and from sudden irregular contractions of the abdominal walls.

Chorion.—The chorion is that portion of the surface of the ovum which does not enter into the formation of the embryo or amnion, and after the separation of the amnion, it forms the whole of the outer surface of the ovum, completely surrounding the embryo, the amnion, and the allantois.

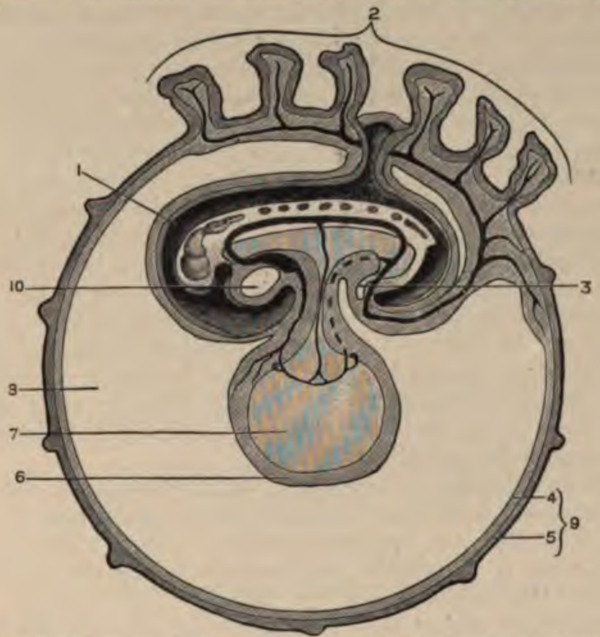

FIG. 637.—Diagram of a longitudinal section of an ovum, showing later stage of formation, amnion and fœtal part of placenta than that shown in fig. 636.

1. Amnion cavity almost completely closed in.
2. Placental villi of chorion.
3. Allantoic diverticulum from cloaca.
4. Epiblast of chorion } 9. Somatopleur.
5. Somatic mesoblast }
7. Yolk sac.
8. Cœlom.
10. Pericardium.

At a very early period its surface is set with fine processes, the *chorionic villi*, which at first consist of epiblastic cells, alone, but very soon they acquire cores of somatic mesoblast, which becomes vascularised by the allantoic vessels which rapidly extend throughout the whole of the chorionic mesoblast.

At first the villi are small, but, as they project into the decidua capsularis and decidua basalis, they grow rapidly and branch repeatedly. Their function is to obtain nutriment from the uterine tissues. In the higher mammals, including man, they destroy and eat up many of the cells of the decidua, and gases and fluids pass through them from the maternal to the fœtal blood, and *vice versâ*. In some mammals, however, they do not destroy the uterine tissues, and in those cases they absorb the uterine milk, which is secreted by the enlarged uterine glands.

The chorionic villi which penetrate the decidua capsularis gradually disappear as the capsularis fuses with the vera, and is reduced to a thin membrane; but the villi which enter the decidua basalis increase enormously in size and complexity, to form the fœtal part of the placenta, and their branches hang free in the interiors of large blood sinuses which are filled with maternal blood (fig. 634).

Allantois.—The allantois is an outgrowth from the ventral portion of the posterior part of the primitive alimentary canal, and it consists of a hollow process of hypoblast covered with mesoblast (fig. 631, 12). In the human embryo it appears at a very early period, before the amnion folds have separated from the chorion, and it conveys the allantoic arteries from the embryo to the chorion, and the allantoic vein from the chorion to the embryo. As development proceeds, and that part of the chorion in contact with the decidua basalis is converted into the fœtal part of the placenta (figs. 634 to 637), the allantoic blood-vessels in the chorion gradually disappear except in the placental area where they grow larger till birth.

At first the allantois is very short, but, as the amnion distends and the embryo passes further and further into the interior of the enlarging ovum, it is elongated into a cord which, together with the remains of the yolk-sac is surrounded and ensheathed by the amnion; this cord is called the *umbilical cord* (fig. 634).

In the human subject that portion of the allantois which lies in the umbilical cord consists entirely of vascular mesoblast, for the hollow pouch of hypoblast ends near the umbilicus; but in some mammals the hypoblastic diverticulum is prolonged to the inner surface of the chorion. In man, therefore, the umbilical cord consists of—1, An outer covering of amnion; 2, a core of modified mesoblast derived from the mesoblast of the allantois and the wall of the yolk-sac; 3, the remains of the hypoblastic portion of the yolk-sac, and 4, the two allantoic arteries and the allantoic vein.

In the early stages immediately after the separation of the amnion from the chorion, the embryo and its amnion are attached to the chorion by the allantois, and they are situated in a space which is part of the original cœlomic space between the somatic and splanchnic mesoblast (figs. 635 to 637). This space is continuous with the cœlum in the embryo at the umbilical orifice. In the later periods it is entirely obliterated, for the amnion is distended till its outer surface fuses with the inner surface of the chorion; and at the same time the umbilical cord is differentiated as the distending amnion surrounds and presses together the allantoic stalk and the remains of the yolk-sac (fig. 634).

At birth, on account of the contraction of the walls of the uterus and the pressure of the surrounding muscles, the liquor amnii forces part of the membrane formed by the fused amnion and chorion through the cervix uteri, which is gradually distended. When the distension is sufficient, the membrane ruptures, the liquor amnii escapes, and afterwards the child is forced out. It still remains connected with the placenta by the umbilical cord, and this connection should not be severed for a few minutes, in order that as much blood as possible may be aspirated from the fœtal part of the placenta into the child as breathing commences.

After the child is expelled the contraction of the uterine wall continues and the placenta is separated and forced out. The separation gradually extends through the decidua, along the line of the stratum spongiosum, and the fused chorion amnion and decidua turned inside out, follow the placenta to which they are attached, constituting, with the placenta, the after-birth.

After the umbilical cord is tied and separated, the umbilical arteries inside the child become filled with blood-clot, and ultimately they are converted into fibrous cords, the so-called obliterated hypogastric arteries, and at the same time the allantois is also converted into a fibrous strand, the urachus, which extends from the apex of the bladder to the umbilicus.

Development of the Framework of the Body.

In the early stages of development, the only indication of a framework or skeleton is the notochordal rod of hypoblastic cells, which extends along the whole length of the dorsal wall of the primitive intestine beneath the neural tube, its anterior end being situated immediately behind the position where the pituitary body is afterwards formed. In mammals the notochord disappears, except in the centres of the intervertebral discs, but in amphioxus and lampreys it persists as a permanent skeletal support, and in these cases it closely resembles cellular cartilage enclosed in a fibrous sheath. It is composed of a very insoluble proteid-like substance, which, however, is not collagen. Collagen and gelatin (which is formed from collagen by boiling), are characteristic of true connective tissues which are formed from mesoblast; the notochord is hypoblastic. The notochord contains also, like all embryonic tissues, a large quantity of glycogen.

The rudiments from which the axial skeleton of the body is formed are the protovertebræ or mesoblastic somites (see p. 833). Each protovertebra separates into three parts:—1. An outer, the cutaneous lamella, from which the deeper parts of the skin and the subcutaneous tissues of the body are developed. 2. A middle portion, the muscle plate. From the muscle plates all the striped muscles of the body, with the exception of those of the heart, are formed. 3. A scleratogenous segment. The scleratogenous segments fuse together round the neural tube and the notochord, and in this way a continuous membranous vertebral column is formed. This is cleft on each side in every segment, for the passage of the nerve-roots and the accompanying blood-vessels. Part of the membranous column is converted first into cartilaginous and afterwards into bony vertebræ; other parts are transformed into intervertebral discs and ligaments, and the remainder forms the membranes which line the spinal canal and surround the spinal cord. From the sides of the vertebræ the

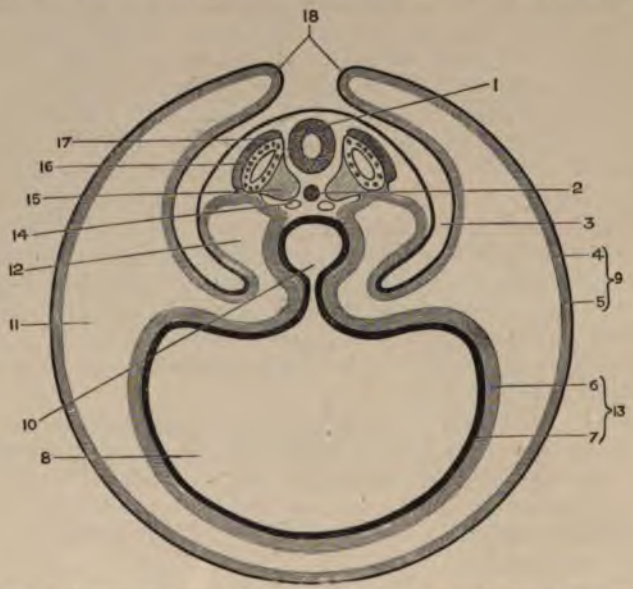

FIG. 638.—Diagram of a transverse section of an ovum showing differentiation of protovertebræ and formation of amnion folds, primitive intestine, and yolk-sac.

1. Spinal cord.
2. Notochord.
3. Amnion cavity.
4. Epiblast
5. Somatic mesoblast } 9. Somatopleur.
6. Splanchnic mesoblast
7. Hypoblast } 13. Splanchnopleur.
8. Yolk-sac.

10. Primitive intestine.
11. Cœlom (extra-embryonic).
12. Cœlom (intra-embryonic).
14. Primitive dorsal blood-vessel.
15. Scleratogenous part of protovertebra.
16. Muscle plate part of protovertebra.
17. Cutaneous lamella of protovertebra.
18. Amnion folds.

ribs grow outwards and forwards in the thoracic region, and some of them meet together in front, and enter into the formation of the sternum or breast-bone.

The Limbs.—At first there are no limbs, and then they jut out as buds from the sides of the body. Each consists of an epiblastic covering and a core of mesoblast. The central part of the mesoblast condenses and forms the cartilaginous rudiments of the bones which afterwards become ossified, and it also forms the ligaments which connect the bones together. Buds from the muscle plates, opposite the limbs, grow into them to form the muscles, and nerves from the corresponding segments of the spinal cord enter the buds (fig. 639). Blood-vessels connected with the vessels of the body also appear.

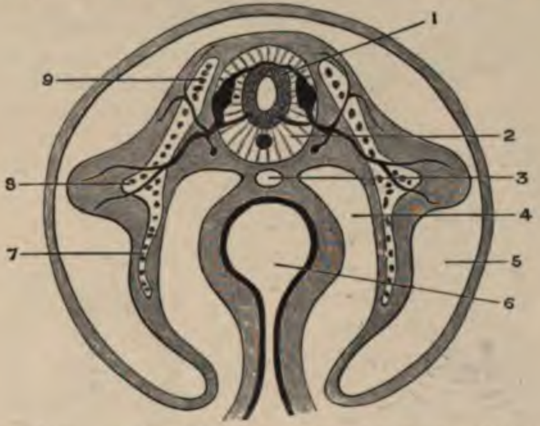

FIG. 639.—Diagram of a transverse section of embryo and amnion, showing extension of muscle plates, rudimentary limbs, and membranous vertebral column. 1, Spinal cord with nerve-roots; 2, membranous vertebral column, formed from fused scleratogenous segments of protovertebræ; 3, descending aorta; 4, cœlom; 5, amnion cavity; 6, primitive intestine; 7, muscle plate extending into body wall; 8, bud of muscle plate into limb; 9, muscle plate.

The Head.—In the early stages the head is merely a rounded projection developed in the head fold of the embryo. Its anterior part is bent sharply downwards in front of the anterior end of the body in which the pericardium has been formed, and the cleft between the front of the head and the pericardium is the stomadœal space or primitive mouth cavity (figs. 640, 641, 642). At this time there is no neck, but from the posterior part of the head to the side of the pericardium, a series of five visceral arches, with four intermediate clefts, extend round the sides of the foregut. As the neck forms, the visceral arches move forward with the head, and their lower ends meet in the middle line of the neck in front of the anterior end of the body; thus it comes about that the stomadœal space is now bounded laterally and below by the first or mandibular arches, and above by the anterior part of the head which is called the fronto-nasal process. The back of the space is bounded for a time by a thin membrane which separates the foregut from the stomadæum. Just in front of the upper end of this membrane a diverticulum projects from the stomadæum towards the brain—this is Rathke's pouch; it meets a downgrowth from the brain called the hypophysis, and the two structures unite to form the two lobes of the pituitary body. The membrane soon disappears, and the primitive mouth and the foregut form a continuous cavity. In the meantime two olfactory pits have appeared on the under surface of the fronto-nasal process, and they grow back into the roof of the stomadæum. These pits cut the fronto-nasal process into three parts, the mesial nasal process between them, and the lateral nasal processes at the sides. Moreover, two little projections, the globular processes, grow down on each side of the middle line from the mesial nasal process. At this period the upper boundary of the orifice of the stomadæum is formed by the two globular processes separated by a small cleft, and the two lateral nasal processes separated from the globular processes by the olfactory

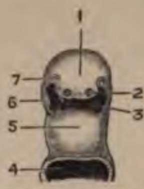

Fig. 640.—Diagram representing front view of anterior part of a very young embryo. 1, Fronto-nasal process of head; 2, olfactory pit; 3, stomadæum; 4, umbilical orifice; 5, pericardium; 6, mandibular arch; 7, eye.

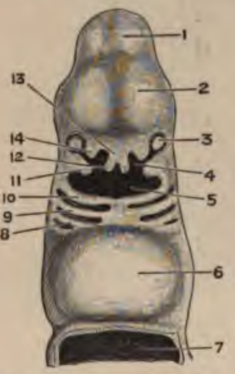

Fig. 641.—Diagram of anterior view of an embryo older than that shown in fig. 640. 1, Mid-brain; 2, fore-brain; 3, eye; 4, olfactory pit; 5, stomadæum; 6, pericardium; 7, umbilical orifice; 8, third visceral arch; 9, second visceral arch; 10, first or mandibular arch; 11, maxillary process of mandibular arch; 12, globular process; 13, mesial nasal process; 14, lateral nasal process.

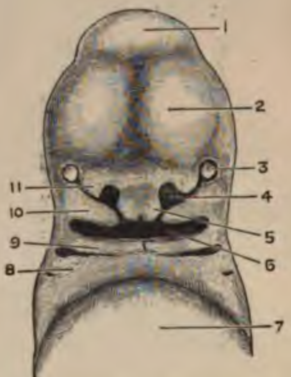

Fig. 642.—Diagram representing a later stage of development of the face than that shown in fig. 641. 1, Mid-brain; 2, fore-brain; 3, eye; 4, anterior nasal orifice; 5, globular process; 6, mouth; 7, pericardium; 8, second visceral arch; 9, first visceral arch; 10, maxillary process of first arch; 11, lateral nasal process.

pits, and the sides and the lower boundary of the orifice are formed by the first or mandibular arches. From the upper ends of the mandibular arches the maxillary processes grow forwards immediately beneath the eyeballs (which have appeared on the sides of the head), and as they grow they pass beneath the lateral nasal processes, and beneath the anterior ends of the olfactory depressions, and fuse with the globular processes which also fuse together. Thus the orifice of the stomadæal space is cut into three parts, the two nasal orifices and the mouth. The upper lip is formed by the fused globular and maxillary processes, and contains three lines of fusion—one in the middle line between the globular processes, and two more laterally placed between the maxillary processes and the globular processes. In certain cases the fusions do not take, and then clefts are left in the upper lip, and constitute the various forms of hare-lip. From the inner parts of the maxillary processes of opposite sides, palatal ledges grow across the stomadæal space; and meeting in the middle line, they fuse together and separate the space into an upper or nasal and a lower or buccal space. If the palatal ledges fail to meet, cleft palate results. A cleft may also appear between the nasal orifice and the conjunctival sac, as a result of the absence of fusion between the maxillary process and the lateral nasal process. The lower boundary of the mouth orifice is formed by the mandibular arches.

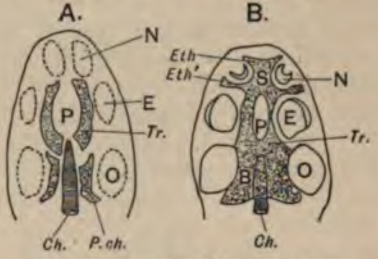

Fig. 643.—Diagrams of the cartilaginous cranium.

A, first stage. *Ch*, Notochord; *Tr*, trabeculæ cranii; *P.ch.*, parachordal cartilages; *P*, situation of pituitary body; *N*, *E*, *O*, situations of olfactory, visual, and auditory organs.
B, later stage. *B*, Basilar cartilages; *S*, nasal septum and ethmoidal cartilages; *Eth*, *Eth'*, prolongations of ethmoid around olfactory organ, completing the nasal capsule; *N*, *E*, *O*, *Ch*, *Tr*, *P*, as before. (After Wiedersheim.)

Both the tissues of the fronto-nasal process and those of the mandibular arches take part in the formation of the skeleton of the head. The notochord extends forwards as far as the pituitary body in all vertebrates, and in some, protovertebral somites can be traced forwards to a similar point; but in mammals they are only distinct behind the ear in the occipital region, and even there they entirely disappear at an early period. In the lower vertebrates a bar of cartilage appears at each side of the notochord in the head; these are the parachordal cartilages, and they soon fuse to form a basilar plate in which the notochord is embedded. It becomes the basi-occipital and basi-sphenoid bones. In mammals, the parachordal stage is eliminated, and a basilar plate is formed at once. In front of the basilar plate two trabeculæ cranii embrace the pituitary body and extend forward into the fronto-nasal process, where they blend together to form an ethmo-vomerine plate; and from this, processes extend down on each side, the nasal part of the stomadæal space forming the rudiments of the ethmoid and inferior turbinal bones, and a mesial process descends into a septum which has grown down from the under surface of the fronto-nasal process, and united with the palate dividing the nasal chamber into right and left halves. In this the vertical plate of the ethmoid and the vomer are ossified. The posterior parts of the trabeculæ fuse with the basilar plate and form the rudiment of the presphenoid. Posteriorly, and at the sides, cartilaginous plates grow over the cerebral vesicles; but in mammals the occipital region alone is roofed in by cartilage; the rest of the cranial vault being formed of membrane bones.

From the sides of the presphenoid, the lesser wings or orbito-sphenoids containing the optic foramina are developed, and from the sides of the basi-sphenoid the greater wings or alisphenoids. A cartilaginous capsule invests the auditory vesicle, and becomes connected to the parachordal cartilage on each side. It is called the periotic capsule; it is replaced by bone, which constitutes the petrous and mastoid portions of the temporal bone.

Cartilaginous bars appear in the visceral arches, and from that in the mandibular arch on each side—Meckel's cartilage;—the symphysis of the jaw, the malleus, and possibly the incus are formed. The stapes is the result of a separate ossification round the stapedial artery. The remainder of the mandible is ossified in the membrane around the mandibular cartilage.

From the second bars the anterior part of the body of the hyoid bone, its small cornua, the stylo-hyoid ligaments, and the styloid processes are developed. The cartilages of the third arches give rise to the posterior part of the body of the hyoid, and its great cornua; the cartilages of the remaining arches take part in the formation of the cartilages of the larynx.

In mammals the clefts between the arches are merely grooves which do not communicate with the cavity of the foregut, as they do in fishes and amphibians. The outer depression of the first cleft forms the external auditory meatus, and the inner depression is converted into the tympanic cavity and the Eustachian tube. The remaining clefts disappear.

The cranial nerves are also associated with the arches and clefts. The third division of the fifth is distributed to the mandibular arch, its second division goes to the maxillary process, and its first division to the fronto-nasal process. The seventh is the nerve of the second arch, the ninth belongs to the third arch, and the remaining arches are associated with the tenth nerve.

Development of the Vascular System.

We have already seen that at an early stage of development, blood-vessels begin to form in the splanchnic mesoblast on the wall of the yolk-sac, outside the embryo, in an area called the area vasculosa. From the cephalic end of this area two longitudinal vessels run backwards through the embryonic region, and they terminate posteriorly in the caudal part of the area vasculosa (fig. 644). As they run through the embryonic region, which is still outspread on the surface of the ovum, they pass beneath the pericardium, and then beneath the inner parts of the protovertebræ, not far from the sides of the notochord. As the head and the tail folds of the embryo form, these longitudinal vascular tubes are bent, both in front and behind, and, after the bending, each consists of five parts. A dorsal part which extends along the dorsal wall of the alimentary canal; two ventral parts, one in front of the umbilicus and one behind that orifice, and two arches, a cephalic and a caudal, connecting the dorsal portion of each vessel with the anterior and posterior ventral portions respectively (fig. 645). The blood flows from the anterior part of the yolk-sac wall into the anterior ventral parts of these primitive embryonic vessels by two channels, which are called the *omphalo-mesenteric veins.* The anterior ventral vessels into which the omphalo-mesenteric veins pass, lie, now that the folding of the embryo has taken place, in the dorsal wall of the

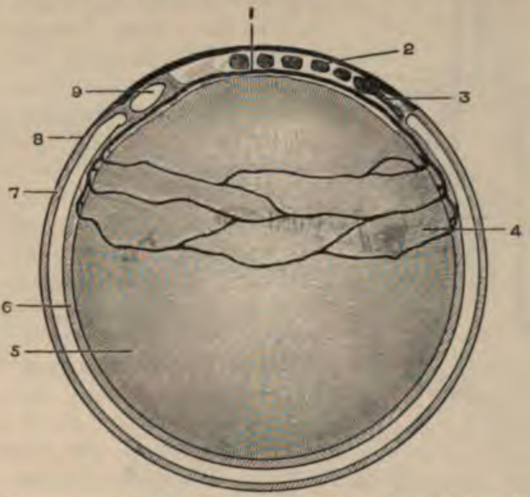

FIG. 644.—Diagram representing the arrangement of the primitive blood-vessels before the embryo is folded off from the ovum. 1, Primitive vessel of left side; 2, protovertebra; 3, primitive streak; 4, vascular area of yolk-sac; 5, non-vascular area of yolk-sac; 6, splanchnic mesoblast; 7, somatic mesoblast; 8, epiblast; 9, pericardium.

pericardium and on the ventral wall of the foregut; they are the primitive heart tubes, and their anterior ends run into the first cephalic aortic arches, which pass round the sides of the anterior end of the foregut into the primitive dorsal vessels. A little later the parts of the anterior ventral vessels in front of the heart are connected with the dorsal vessels by four additional arches, one in each visceral arch—that is, there are now five aortic arches on each side connecting the anterior parts of the ventral with the anterior parts of the dorsal vessels. The portions of the ventral vessels which lie behind the arches in the dorsal wall of the pericardium rapidly enlarge, and they fuse together to form the single heart, which is thus for a time a single longitudinal vessel. The parts of the ventral and dorsal vessels immediately behind each arch are called the roots of the arch.

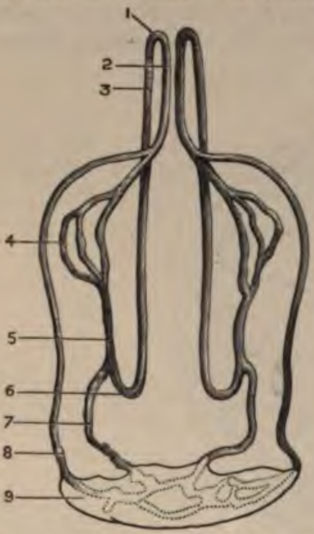

FIG. 645.—Diagram representing the primitive blood-vessels of the embryo. 1, First cephalic aortic arch; 2, anterior ventral part of primitive vessel; 3, dorsal part of primitive vessel; 4, vascular area of yolk-sac; 5, posterior ventral part of primitive vessel; 6, caudal aortic arch; 7, allantoic or umbilical branch; 8, umbilical or allantoic vein; 9, placenta.

In mammals, the first and second arches disappear, and their ventral roots become the external carotid artery. The third arches and the dorsal roots of the first and second arches form the internal carotids. The dorsal root of the third arch disappears on each side, and the ventral root forms the common carotid artery. The ventral root of the right fourth arch becomes the innominate artery, and the arch itself takes part in the formation of the right subclavian artery. The dorsal roots of the right fourth and fifth arches and the dorsal part of the fifth arch itself disappear, and the ventral part of the fifth arch becomes the right pulmonary artery. The left fourth arch, with its dorsal and ventral roots, and the dorsal root of the left fifth arch, take part in the formation of the arch of the aorta. The left fifth arch persists till birth, then its dorsal part becomes a fibrous cord, the ligamentum arteriosum, and its ventral part forms the left pulmonary artery (fig. 647).

The five aortic arches correspond with the gill arteries of fishes, but in mammals they never break up into capillaries, as in the fishes' gills. In amphibia three pairs persist throughout life. In reptiles the fourth pair remains throughout life as the permanent right and left aortæ. In birds the right fourth remains as the permanent aorta, curving over the right bronchus, whereas in mammals, the left fourth arch becomes the permanent aorta, curving over the left bronchus.

Behind the dorsal roots of the fifth arches the dorsal longitudinal vessels fuse together, as far back as the lumbar region, to form the descending aorta, and the lower or posterior end of this vessel is continued at first through the caudal arches into the posterior ventral portions of the longitudinal vessels which end on the yolk-sac (fig. 646). As soon as the allantois forms, each of the posterior ventral vessels gives off a large branch to it, and in front of the origin of this vessel it atrophies so that now the dorsal vessels are continued through the caudal arches into the allantoic or umbilical arteries, which carry blood to the placenta, and new vessels of small size are given off from the descending aorta to the yolk-sac. A little later the primary caudal arches, which lie inside the posterior ends of the Wolffian ducts, are replaced by new arches, which pass outside the ducts, and connect the posterior ends of the dorsal longitudinal vessels with the allantoic arteries. At the same time the hind limbs appear, and each receives a branch from the corresponding dorsal vessel; this is the external iliac artery. After its appearance the part of the dorsal vessel between it and the aorta is the common iliac artery, and the portion of the dorsal vessel behind it, together

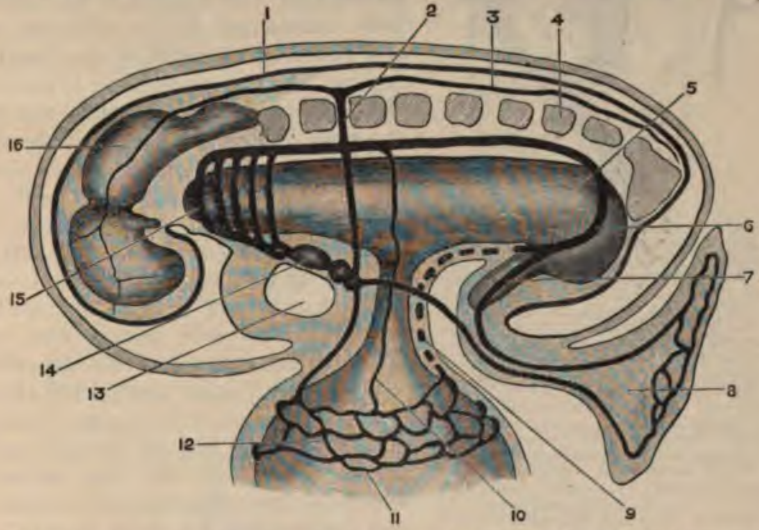

FIG. 646.—Diagram representing arrangement of primitive blood-vessels of left side of embryo. 1, Left primitive jugular vein; 2, left duct of Cuvier; 3, left cardinal vein; 4, protovertebra; 5, primitive intestine; 6, caudal aortic arch; 7, allantoic or umbilical artery; 8, placenta; 9, atrophied posterior ventral part of primitive vessel; 10, yolk-sac artery; 11, yolk-sac; 12, vascular area on yolk-sac; 13, pericardium; 14, heart; 15, cephalic aortic arch; 16, brain.

with the caudal arch, becomes the internal iliac or hypogastric artery. This is continued in the embryo along the ventral wall of the body as the umbilical arteries to the placenta.

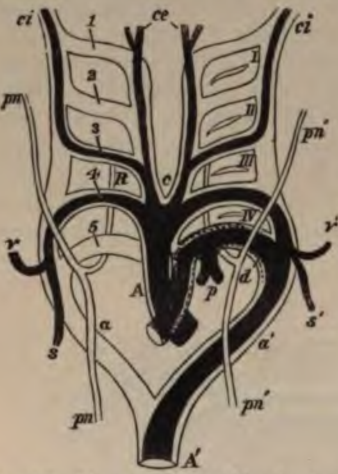

FIG. 647.—Diagram of the aortic arches in a mammal, showing transformations which give rise to the permanent arterial vessels. *A*, Primitive arterial stem or aortic bulb, now divided into *A*, the ascending part of the aortic arch, and *p*, the pulmonary; *a a'*, right and left aortic roots; *A'*, descending aorta; 1, 2, 3, 4, 5, the five primitive aortic or branchial arches; *I*, *II*, *III*, *IV*, the four branchial clefts which, for the sake of clearness, have been omitted on the right side. The permanent systemic vessels are deeply, the pulmonary arteries lightly, shaded; the parts of the primitive arches which are transitory are simply outlined; *c*, placed between the permanent common carotid arteries; *c e*, external carotid arteries; *c i*, internal carotid arteries; *s*, right subclavian, rising from the right aortic root beyond the fifth arch; *v*, right vertebral from the same, opposite the fourth arch; *v' s'*, left vertebral and subclavian arteries rising together from the left, or permanent aortic root, opposite the fourth arch; *p*, pulmonary arteries rising together from the left fifth arch; *d*, outer or back part of left fifth arch, forming ductus arteriosus; *p n*, *p n'*, right and left pneumogastric nerves descending in front of aortic arch, with their recurrent branches represented diagrammatically as passing behind, to illustrate the relations of these nerves respectively to the right subclavian artery (4) and the arch of the aorta and ductus arteriosus (*d*). (Allen Thomson, after Rathke.)

The Heart.—The simple longitudinal heart soon becomes separated by three transverse constrictions into four chambers, which are, from behind forwards, the sinus venosus, the auricle, the ventricle, and the aortic bulb (figs. 648 and 649). The sinus venosus receives the omphalo-mesenteric and other veins, and the aortic bulb terminates in the fifth arches and the ventral roots of the fourth arches. The sinus venosus is gradually absorbed into the auricle, and at the same time the heart tube bends so that the auricle is placed behind the ventricle and the aortic bulb—that is, between them and the wall of the foregut (figs. 650 and 651). As soon as the bending is completed each chamber is divided by septa into right and left halves, but an opening, the foramen ovale, remains in the interauricular septum till after birth. The aortic bulb is also divided into two parts: one of these is connected above with the fifth arches, which become the pulmonary arteries, and below with the right ventricle; it becomes, therefore, the stem of the pulmonary artery. The other part, which is connected with the roots of the fourth arches above and the left ventricle below, forms the ascending part of the aorta.

The Veins.—1. The veins of the embryo are the omphalo-mesenteric, which carry blood from the yolk-sac to the heart. 2. The umbilical or allantoic, bearing oxygenated blood from the placenta to the heart. 3. The primitive jugular veins, one on each side returning blood from the head, neck, and upper extremities. 4. The cardinal veins returning blood from the body walls, the

Wolffian bodies, and the hind limbs. 5. The ducts of Cuvier, each of which receives a primitive jugular and a cardinal vein, and ends in the auricle. Thus six veins terminate in the sinus venosus, and through it in the auricle (fig. 648). Both ducts of Cuvier retain their connection with the auricle, the right forming the lower part of the superior vena cava, and the left the oblique vein of Marshall in man, and the lower part of the left superior cava in some mammals.

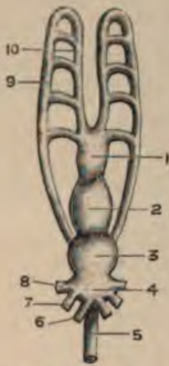

Fig. 648.—Diagram representing an anterior view of the primitive heart, aortic arches, and their roots. 1, Bulbus arteriosus; 2, ventricle; 3, auricle; 4, sinus venosus; 5, descending aorta; 6, omphalo-mesenteric vein; 7, umbilical vein; 8, duct of Cuvier; 9, dorsal roots of aortic arches; 10, ventral roots of aortic arches.

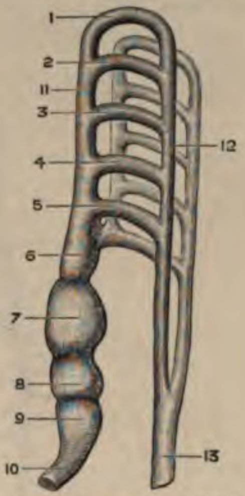

Fig. 649.—Diagram representing a side view of the primitive heart with the cephalic aortic arches and their roots. 1, First cephalic aortic arch; 2, second cephalic aortic arch; 3, third cephalic aortic arch; 4, fourth cephalic aortic arch; 5, fifth cephalic aortic arch; 6, bulbus arteriosus; 7, ventricle; 8, auricle; 9, sinus venosus; 10, omphalo-mesenteric vein (left); 11, ventral roots of aortic arches; 12, dorsal roots of aortic arches; 13, descending aorta.

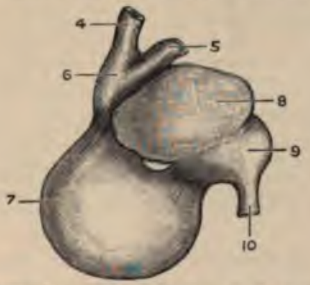

Fig. 650.—Diagram representing a side view of heart after it has folded on itself. 4, Ventral root of fourth aortic arch; 5, fifth aortic arch; 6, bulbus arteriosus; 7, ventricle; 8, auricle; 9, sinus venosus; 10, left omphalo-mesenteric vein.

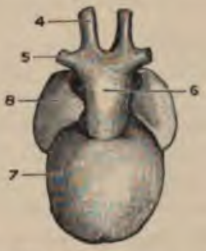

Fig. 651.—Diagram representing an anterior view of the heart after it has folded on itself. 4, Ventral root of fourth aortic arch; 5, fifth aortic arch; 6, bulbus arteriosus; 7, ventricle; 8, auricle.

The upper part of the primitive jugular vein on each side becomes the internal jugular. The lower part on the right side becomes the right innominate vein, and the upper portion of the superior vena cava. On the left side the lower part helps to form the left superior intercostal vein.

The left innominate vein is a transverse anastomosis between the primitive jugular veins. The subclavian veins and the external jugular veins are new formations, the former being developed in association with the growth of the upper limbs.

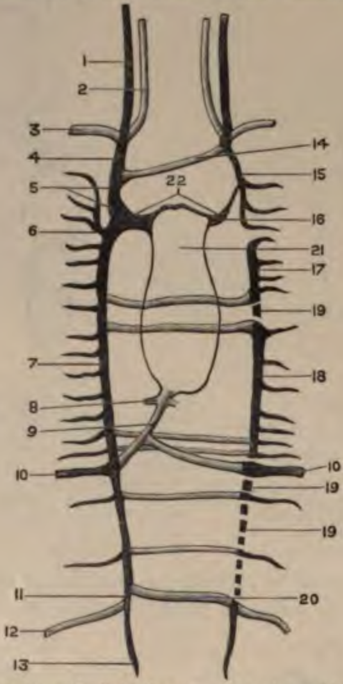

FIG. 652.—The dark are the primitive, the light the secondary veins, with the exception of the external and internal jugular veins. The dark portions entering the auricles are the remains of the primitive ducts of Cuvier. The dark portion above each duct of Cuvier, as far as the external and internal jugular veins, is the primitive jugular vein, and the dark portion below the duct of Cuvier is the cardinal vein. 1, External jugular vein; 2, internal jugular vein; 3, subclavian vein; 4, right innominate vein; 5, superior vena cava; 6, right superior intercostal vein; 7, vena azygos major; 8, right hepatic vein; 9, upper part of inferior vena cava; 10, renal vein; 11, right common iliac vein; 12, right external iliac vein; 13, right internal iliac vein; 14, left innominate vein; 15, left superior intercostal vein; 16, oblique vein of Marshall; 17, vena azygos minor superior; 18, vena azygos minor inferior; 19, atrophied part of left cardinal vein; 20, left common iliac vein; 21, auricle; 22, duct of Cuvier.

The cardinal veins receive the intercostal and lumbar veins from the walls of the body, and the veins from the Wolffian bodies and kidneys. Below the point of union with the external iliac vein from the hind limb the cardinal vein becomes the internal iliac vein. Above the external iliac vein the right cardinal vein forms the right common iliac vein, and the lower part of the inferior vena cava below the right renal vein. Above the right renal vein it becomes the vena azygos major. The parts of the left cardinal between the left lumbar veins disappear, and blood from the left lumbar veins and the left common iliac vein is carried across to the right cardinal, and subsequently to the inferior vena cava by a series of transverse anastomosing channels, of which the lowest becomes the left common iliac vein. The upper part of the left cardinal vein is also broken up, and its remains form the vertical parts of the minor azygos veins and lower part of the left superior intercostal vein. The transverse parts of the minor azygos veins are also developed from transverse anastomosing channels (fig. 652).

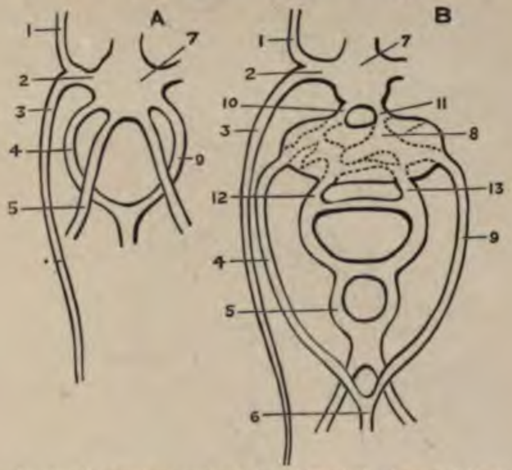

FIG. 653.—Diagram showing the arrangement and transformation of some of the primitive veins. A, Early stage; B, later stage. 1, Primitive jugular vein; 2, duct of Cuvier; 3, cardinal vein; 4, right umbilical vein; 5, right omphalo-mesenteric vein; 6, common umbilical vein; 7, sinus venosus; 8, liver; 9, left umbilical vein; 10, right vena revehens; 11, left vena revehens; 12, right vena advehens; 13, left vena advehens.

In the early stages both the omphalo-mesenteric and the right and left terminal branches of the umbilical vein end in the heart. When the liver forms, the omphalo-mesenteric veins end in venæ advehentes, which break up into capillaries in the liver, and the capillaries end in venæ revehentes, which become the hepatic veins (fig. 653). The left hepatic vein joins the right hepatic vein to form a common trunk, which becomes the upper end of the inferior vena cava, and this is prolonged down to unite with the right cardinal at the level of the right renal vein; but before joining the right cardinal it gives off a branch to join the left cardinal at the level of the left renal vein, and thus the blood from both kidneys enters the inferior vena cava. In the meantime two transverse anastomoses have formed between the omphalo-mesenteric veins below the liver, and still lower the two veins fuse together; thus two loops are formed through which the duodenum passes. The veins from the intestine open into the fused trunks, and the splenic vein enters the left vein at the level of the lower transverse anastomosis. Subsequently the left side of the upper and the right side of the lower loop disappear, and the portal vein is produced from the remains. In the meantime the right umbilical vein has disappeared, and the left has united with the left omphalo-mesenteric vein at the point where the latter ends in the left vena advehens. From this point a direct channel opens up beneath the liver to the upper part of the inferior vena cava; this is the ductus venosus, and it conducts the greater part of the oxygenated blood from the umbilical vein directly to the inferior vena cava, and so to the right auricle; but part of the umbilical blood passes into the liver with the omphalo-mesenteric blood.

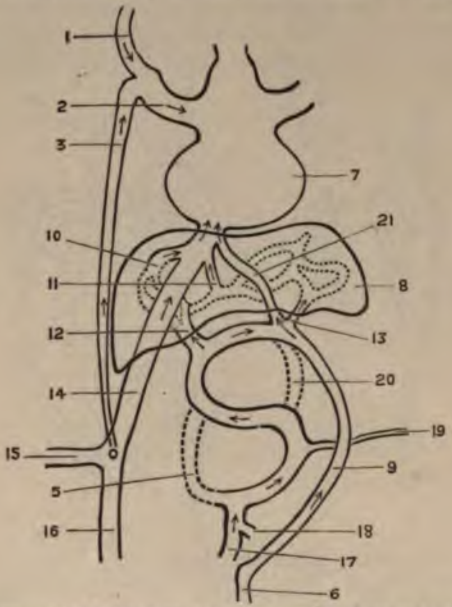

FIG. 654.—Diagram representing a later stage in the development of the veins than that shown in fig. 653. 1, Primitive jugular vein; 2, duct of Cuvier; 3, upper part of cardinal vein, now vena azygos major; 5, remains of light lower limb of loop formed by fusion of omphalo-mesenteric veins; 6, common umbilical vein; 7, sinus venosus; 8, liver; 9, left branch of umbilical vein; 10, right hepatic vein; 11, left hepatic vein; 12, right vena advehens; 13, left vena advehens; 14, upper part of inferior vena cava; 15, right renal vein; 16, lower part of inferior vena cava (cardinal vein); 17, fused part of omphalo-mesenteric vein; 18, vein from alimentary canal; 19, splenic vein; 20, remains of left upper limb of loop formed by fusion of omphalo-mesenteric veins; 21, ductus venosus.

A pulmonary vein forms and carries blood from the lungs to the left auricle. It is subsequently replaced first by two veins, one from each lung, and afterwards four veins, two from each lung.

Circulation of Blood in the Fœtus

The circulation of blood in the fœtus differs considerably from that of the adult. It will be well, perhaps, to begin its description by tracing the course of the blood, which, after being carried to the placenta by the two umbilical arteries, has returned, oxygenated and replenished, to the fœtus by the umbilical vein.

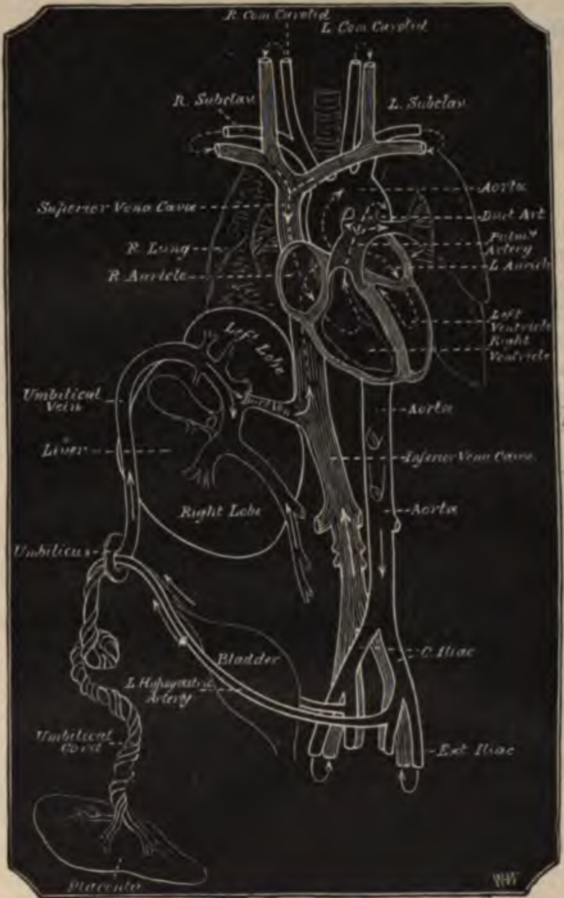

Fig. 655.—Diagram of the Fœtal Circulation.

It is at first conveyed to the under surface of the liver, and there the stream is divided,—a part of the blood passing straight on to the inferior vena cava, through a venous canal called the *ductus venosus*, while the remainder passes into the portal vein, and reaches the inferior vena cava after circulating through the liver. Whether, however, by the direct route through the ductus venosus or by the roundabout way through the liver,—all the blood which is returned from the placenta by the umbilical vein reaches the inferior vena cava at last, and is carried by it to the right auricle of the heart, into which cavity is also pouring the blood that has circulated in the head and neck and arms, and has been brought to the auricle by the superior vena cava. It might be naturally expected that the two streams of blood would be mingled in the right auricle, but such is not the case, or only to a slight extent. The blood from the superior vena cava—the less pure fluid of the two—passes almost exclusively into the right ventricle, through the auriculo-ventricular opening, just as it does in the adult; while the blood of the inferior vena cava is directed by the fold of the lining membrane of the heart, called the *Eustachian valve*, through the foramen ovale into the left auricle, whence it passes into the left ventricle, and out of this into the aorta, and thence to all the body, but chiefly to the head and neck. The blood of the superior vena cava, which, as before said, passes into the right ventricle, is sent out thence in *small amount* through the pulmonary artery to the lungs, and thence to the left auricle, by the pulmonary veins, as in the adult. The greater part, however, does not go to the lungs, but instead, passes through a canal, the *ductus arteriosus*, leading from the pulmonary artery into the aorta just below the origin of the three great vessels which supply the upper parts of the body; and there meeting that part of the blood of the inferior vena cava which has not gone into these large vessels, it is distributed with it to the trunk and other parts—a portion passing out by way of the two umbilical *arteries* to the placenta. From the placenta it is returned by the umbilical *vein* to the under surface of the liver, from which the description started.

Changes after Birth.—Immediately after birth the foramen ovale begins to close, and so do the ductus arteriosus and ductus venosus, as well as the umbilical vessels; the closure is completed in a few days, so that the circulation then takes the course it traverses for the rest of life.

Development of the Nervous System.

The nervous system originates from the thickened walls of the medullary groove, which by the meeting of the dorsal ridges is converted into the medullary canal. These walls are composed entirely of epiblast. The anterior part of this mass becomes the brain, the rest of it the spinal cord; the canal itself is seen in the adult as the ventricles of the brain and central canal of the spinal cord. The nerves are formed of epiblast too; they are outgrowths from masses of cells called neuroblasts, the primitive nerve-cells. In the case, however, of the olfactory and optic nerves we have not to deal with solid outgrowths, but with hollow protrusions from the brain, which become solid at a later stage.

The Spinal Cord.—The cavity formed by the closure of the neural canal soon becomes a cleft running from before backwards. It is bounded at first by columnar epithelium; these cells afterwards become ciliated; on their exterior is a homogeneous basement membrane. The wall soon becomes thicker, and the basement membrane is thus separated further and further from the central canal. This increase in thickness is due in part to the increase in length of the columnar cells: in part to the appearance of new cells. The inner part of the columnar lining retains its palisade-like character, and forms ultimately the lining epithelium of the central canal. The cells are called *spongioblasts.* The external ends of the cells break up into a reticulum called the *myelospongium*, and this is limited externally by the basement membrane at the circumference. The myelospongium forms the neuroglia.

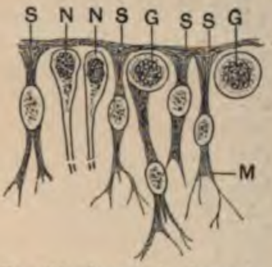

FIG. 656.—Inner ends of spongioblasts (S), with germinal cells (G) between them. NN, neuroblasts which have resulted from the division of a germinal cell; M, myelospongium formed by the branching outer ends of the spongioblasts. (After His.)

Between the inner ends of the spongioblasts (fig. 656, S) numerous rounded cells called *germinal cells* (G) next appear. These rapidly divide, and so form *neuroblasts* (N). The neuroblasts are pear-shaped; each has a large oval nucleus, and its tapering stalk is directed towards the outer surface of the cord; the process ultimately pierces the basement membrane (fig. 657). These are the primitive nerve-cells; their processes are the axis cylinder processes which grow out as nerve-fibres. The nerve sheaths are formed later (see pp. 692-697).

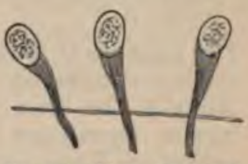

FIG. 657.—Three neuroblasts, each with a nerve-fibre process, growing out beyond the basement membrane of the embryonic spinal cord. (After His.)

The neuroblasts collect into groups, one of which, especially large, is at the situation of the future anterior horn; the processes of the primitive nerve-cells pass out of the cord as the beginnings of the anterior roots (fig. 658). The somewhat oblique coursing of these fibres before they leave the cord forms the beginning of the anterior white column. The posterior white columns simultaneously begin to appear on each side of the narrow dorsal part of the canal. They are formed by the posterior roots entering the cord.

As the cornua of grey matter grow out from the central mass, the anterior fissure and the posterior septum of the cord begin to appear. The anterior or ventral fissure is simply a cleft between the enlarging lateral halves of the cord. The posterior septum is formed by a condensation of the neuroglia in the dorsal wall of the neural canal.

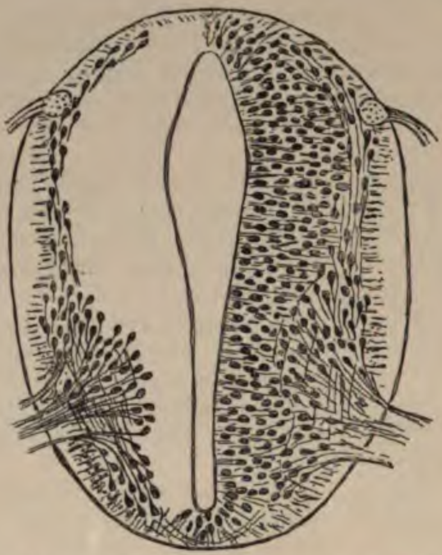

FIG. 658.—Section of spinal cord of a four weeks human embryo. The posterior roots are continued within the cord into a small longitudindal bundle, which is the rudiment of the posterior white column. The anterior roots are formed by the convergence of the processes of the neuroblasts. The latter, along with the elongated cells of the myelospongium, compose the grey matter. (His.)

The cylindrical form of the cord is attained by the development of the lateral columns, which are formed by the processes from neuroblasts in the brain growing down the sides of the cord, and these become medullated at a later period. The membranes and blood-vessels are formed from mesoblast.

Up to the fourth month the cord and vertebral canal increase in length *pari passu*, but after that, the vertebral canal grows faster, so that at birth the coccygeal end of the cord is opposite the third lumbar, and in the adult opposite the first lumbar vertebra. This gives an obliquity to the lower nerve roots, which, together with the *filum terminale*, form the *cauda equina*.

The Nerves.—Some fibres grow from the spinal cord and form the anterior roots which we have already considered. The posterior roots are formed in the following way:—

Along the dorsal aspect of the primitive cord a crest of epiblast appears, and is called the *neural crest*. Special enlargements of this appear opposite the middle of each pair of protovertebræ; these grow downwards on each side, and their attachment to the cord is then entirely lost. These little islands of epiblast contain numerous neuroblasts; each island forms a spinal ganglion, and the neuroblasts within it become the cells of that ganglion. Two processes grow from each cell; one directed towards the spinal cord, where it contributes to the formation of the posterior white column, and ultimately arborises around the cells of the grey matter at a higher level. The other grows to the periphery. The two processes become blended in the first part of their course, and so the T-shaped junction is formed (fig. 659). Small portions segmented off from the spinal ganglia form the sympathetic ganglia.

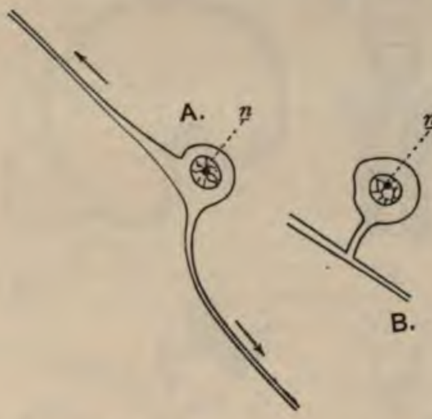

FIG. 659.—A, Bipolar cell from spinal ganglion of a 4½ weeks embryo (after His). *n*, Nucleus; the arrows indicate the direction in which the nerve processes grow, one to the spinal cord, the other to the periphery. B, a cell from a spinal ganglion of the adult; the two processes have coalesced to form a T-shaped junction. (Diagrammatic.)

The Brain.—The histological details of the formation of the epithelium of the ventricles from spongioblasts, of neuroglia from the myelospongium, of nerve-cells from neuroblasts, and of the nerve-fibres of the white matter and of the nerves as the outgrowths from the neuroblasts, are all essentially the same, as already described in connection with the spinal cord. But the grosser anatomical details differ.

The front portion of the medullary canal is almost from the first widened out and divided into three vesicles. From the anterior vesicle the two primary optic vesicles are budded off laterally: their further history will be traced in the next section. Somewhat later the same vesicle divides into two, and thus the telencephalon and diencephalon are formed.

In the walls of the posterior (third) cerebral vesicle, a thickening appears (rudimentary cerebellum) which becomes separated from the rest of the vesicle by a deep inflection.

At this time there are two chief curvatures of the brain (fig. 660).

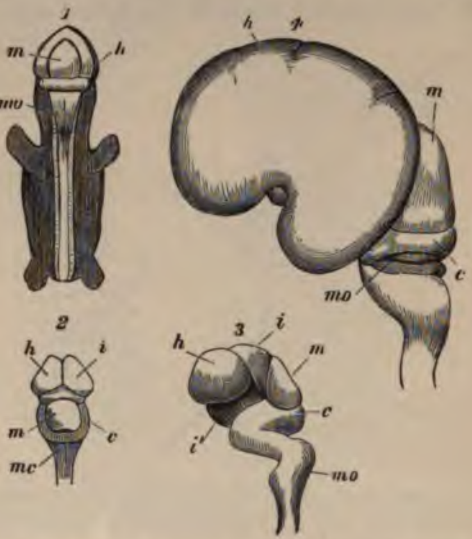

FIG. 660.—Early stages in development of human brain (magnified). 1, 2, 3, are from an embryo about seven weeks old; 4, about three months old. *m*, Middle cerebral vesicle (mesencephalon); *c*, cerebellum; *m o*, medulla oblongata; *i* (in fig. 3), diencephalon; *h*, telencephalon; *i'*, infundibulum; fig. 3 shows the several curves which occur in the course of development; fig. 4 is a lateral view, showing the great enlargement of the cerebral hemispheres which have covered in the thalami, leaving the optic lobes, *m*, uncovered. (Kölliker.)

N.B.—In fig. 2 the line *i* terminates in the right hemisphere; it ought to be continued into the diencephalon.

(1.) A sharp bend of the whole cerebral mass downwards round the end of the notochord, by which the anterior vesicle, which was the highest of the three, is bent downwards, and the middle one comes to occupy the highest position. (2.) A sharp bend, with the convexity forwards, which runs in beneath the rudimentary cerebellum separating it from the medulla.

Thus, five fundamental parts of the fœtal brain may be distinguished, which, together with the parts developed from them, may be presented in the following tabular view:—

TABLE OF PARTS DEVELOPED FROM FUNDAMENTAL PARTS OF BRAIN.

I. Anterior Primary Vesicle.	First Secondary Vesicle, Telencephalon, or Fore-brain.	Anterior end of third ventricle, foramen of Monro, lateral ventricles, cerebral hemispheres, corpora striata corpus callosum, fornix, lateral ventricles, olfactory bulb.	
	Second Secondary Vesicle, Diencephalon, or 'Twixt-brain.	Thalami optici, pineal gland, part of pituitary body, third ventricle, optic nerve and retina, infundibulum.	
II. Middle Primary Vesicle.	Third Secondary Vesicle, Mesencephalon, or Mid-brain.	Corpora quadrigemina, crura cerebri, aqueduct of Sylvius.	
III. Posterior Primary Vesicle.	Fourth Secondary Vesicle, or Metencephalon.	Fourth ventricle.	Cerebellum and Pons.
	Fifth Secondary Vesicle, or Myelencephalon.	Fourth ventricle.	Medulla oblongata.

The cerebral hemispheres formed by bifurcation of the telencephalon grow rapidly upwards and backwards, while from their inferior surfaces the olfactory bulbs are budded off. The middle cerebral vesicle (mesencephalon) for some time is the most prominent part of the fœtal brain, and in fishes, amphibia, and reptiles, it remains uncovered through life as the optic lobes. But in birds the growth of the cerebral hemispheres thrusts the optic lobes down laterally, and in mammalia completely overlaps them.

In the lower mammalia the backward growth of the hemispheres ceases, but in the higher groups, such as the monkeys and man, they grow still further back, until they completely cover in the cerebellum, so that on looking down on the brain from above, the cerebellum is quite concealed from view. The surface of the hemispheres is at first quite smooth, but as early as the third month the great Sylvian fissure begins to be formed (fig. 661).

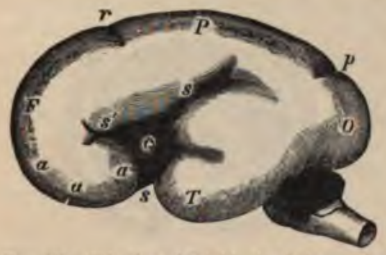

FIG. 661.—Side view of fœtal brain at six months, showing commencement of formation of the principal fissures and convolutions. *F*, Frontal lobe; *P*, parietal; *O*, occipital; *T*, temporal; *a a a*, commencing frontal convolutions; *s*, Sylvian fissure; *s'*, its anterior division; *c*, within it the central lobe or island of Reil; *r*, fissure of Rolando; *p*, parieto-occipital fissure. (R. Wagner.)

The next to appear is the parieto-occipital fissure; these two great fissures, unlike the rest of the sulci, are formed by a curving round of the whole cerebral mass.

In the sixth month the fissure of Rolando appears: from this time till the end of fœtal life the brain grows rapidly in size, and the convolutions appear in quick succession; first the great primary ones are sketched out, then the secondary ones. The commissures of the brain, and the corpus callosum, are developed by the growth of fibres across the middle line.

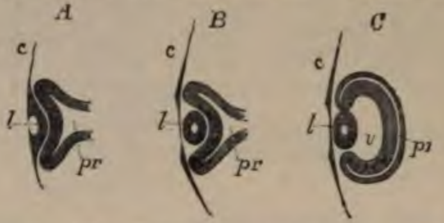

FIG. 662.—Longitudinal section of the primary optic vesicle in the chick, magnified (from Remak).—A, from an embryo of sixty-five hours; B, a few hours later; C, of the fourth day; *c*, the corneous layer or epidermis, presenting in A the open depression for the lens, which is closed in B and C; *l*, the lens follicle and lens; *pr*, the primary optic vesicle; in A and B, the pedicle which forms the optic nerve is shown; in C, the section being to the side of the pedicle, the latter is not shown; *v*, the secondary optic vesicle and vitreous humour.

The Hippocampus major is formed by the folding in of the grey matter from the exterior into the lateral ventricles.

The Eye.—Soon after the first three cerebral vesicles have become distinct from each other, the anterior one sends out a lateral vesicle from each side (primary optic vesicle), which grows out towards the free surface, its cavity communicating with that of the

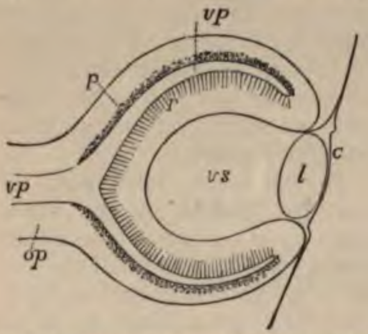

FIG. 663.—Diagrammatic sketch of a vertical longitudinal section through the eyeball of a human fœtus of four weeks. The section is a little to the side, so as to avoid passing through the ocular cleft; *c*, the cuticle where it becomes later the corneal epithelium; *l*, the lens; *op*, optic nerve formed by the pedicle of the primary optic vesicle; *vp*, primary medullary cavity or optic vesicle; *p*, the pigment layer of the retina; *r*, the inner wall forming the remaining layers of the retina; *vs*, secondary optic vesicle containing the rudiment of the vitreous humour. × 100. (Kölliker.)

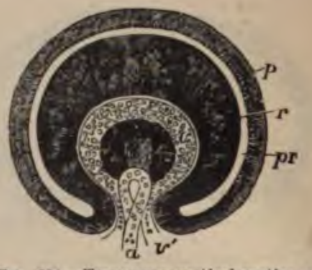

FIG. 664.—Transverse vertical section of the eyeball of a human embryo of four weeks. The anterior half of the section is represented: *pr*, the remains of the cavity of the primary optic vesicle; *p*, the inner part of the outer layer forming the retinal pigment; *r*, the thickened inner part giving rise to the other structures of the retina; *v*, the commencing vitreous humour within the secondary optic vesicle; *v′*, the ocular cleft through which the loop of the central blood-vessel, *a*, projects from below; *l*, the lens with a central cavity. × 100. (Kölliker.)

cerebral vesicle through the canal in its pedicle. It remains connected to the diencephalon. It is soon met and invaginated by an ingrowing process from the epiblast of the surface (fig. 662). This process of the epiblast is at first a depression, which ultimately becomes closed in at the edges so as to produce a hollow ball, which is thus completely severed from the epidermis with which it was originally continuous. From this hollow ball the crystalline lens is developed. The way in which this occurs has been described in a previous chapter (see p. 770). By the ingrowth of the lens the anterior wall of the primary optic vesicle is forced back nearly into contact with the posterior, and thus the primary optic vesicle is almost obliterated. The cells in the anterior wall are much longer than those of the posterior wall; from the former all the layers of the retina are developed, except the layer of pigment cells which is formed from the latter.

The cup-shaped hollow in which the lens is now lodged is termed the secondary optic vesicle; its walls grow up all round, leaving, however, a slit below where it meets the lens. This slit is the choroidal fissure.

The cavity of the secondary optic cup is filled by processes of the neuroglia cells of the retina. Amidst these a process of vascular mesoblast projects through the choroidal fissure, and by the union of the two the vitreous humour, the lens capsule, and the capsulo-pupillary membrane are formed. In mammals the mesoblastic process projects, not only into the secondary optic vesicle, but also into the pedicle of the primary optic vesicle, invaginating it for some distance from beneath, and thus carrying up the *arteria centralis retinæ* into its permanent position in the centre of the optic nerve.

This invagination of the optic nerve does not occur in *birds*, and consequently no arteria centralis retinæ exists in them. But they possess an important permanent relic of the original protrusion of the mesoblast through the choroidal fissure, in the *pecten*, while a remnant of the same fissure sometimes occurs in man under the name coloboma iridis. The cavity of the primary optic vesicle becomes completely obliterated, and the rods and cones get into apposition with the pigment layer of the retina. The inner segments of the rods are the first formed, then the outer. The cavity of its pedicle disappears and the solid optic nerve is formed. Meanwhile the cavity in the centre of the primitive lens becomes filled up by the growth of fibres from its posterior wall. The epithelium of the cornea is developed from the epiblast, while the corneal tissue proper is derived from the mesoblast which intervenes between the epiblast and the primitive lens which was originally continuous with it. The *sclerotic* coat is developed round the eyeball from the general mesoblast in which it is imbedded. The *choroid* is developed from the mesoblast on the outside of the optic cup, and the iris by the growing forwards of the anterior edge of the optic cup. The ciliary processes arise from the hypertrophy of the edge of the optic cup, which forms folds into which the choroidal mesoblast grows, and in which blood-vessels and pigment-cells develop.

The iris is formed rather late, as a circular septum projecting inwards, from the fore part of the choroid, between the lens and the cornea. In the eye of the fœtus of mammalia, the pupil is closed by a delicate membrane, the *membrana pupillaris,* which forms the front portion of a highly vascular membrane that, in the fœtus, surrounds the lens, and is named the *membrana capsulo-pupillaris* (fig. 665). It is supplied with blood by a branch of the *arteria centralis retinæ,* which, passing forwards to the back of the lens, there subdivides. The arteria centralis is obliterated in the adult, and is then called the canal of Stilling. The membrana capsulo-pupillaris disappears in the human subject a short time before birth.

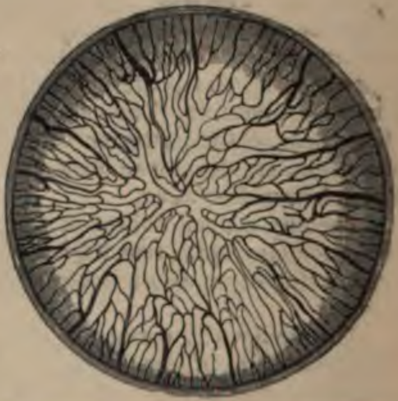

FIG. 665.—Blood-vessels of the capsulo-pupillary membrane of a new-born kitten (magnified). The drawing is taken from a preparation injected by Tiersch, and shows in the central part the convergence of the net-work of vessels in the pupillary membrane. (Kölliker.)

The eyelids of the human subject and mammiferous animals, like those of birds, are first developed in the form of a ring. They then extend over the globe of the eye until they meet and become firmly agglutinated to each other. But before birth, or in the carnivora after birth, they separate.

The Ear.—Very early in the development of the embryo a depression or ingrowth of the epiblast occurs on each side of the head, which deepens and soon becomes a closed follicle. This *primary otic vesicle,* which closely corresponds in its formation to the lens follicle in the eye, sinks down to some distance from the free surface from it are developed the epithelial lining of the *membranous* labyrinth of the internal ear, consisting of the vestibule and its semicircular canals and the scala media of the cochlea. The surroundin mesoblast gives rise to the various fibrous bony and cartilagino parts which complete and enclose this membranous labyrinth, t bony semicircular canals, the walls of the cochlea with its scala ves buli and scala tympani.

The Eustachian tube, the cavity of the tympanum, and external auditory passage, are the remains of the first or hyomandibular cleft. The membrana tympani divides the cavity of this cleft into the tympanum, and the external meatus. The mucous membrane of the pharynx, which is prolonged in the form of a diverticulum through the Eustachian tube into the tympanum, and the external cutaneous system come into relation with each other at this point; the two structures are separated only by the membrane of the tympanum.

The pinna or external ear is developed from a process of integument in the neighbourhood of the first and second visceral arches, and probably corresponds to the gill-cover (operculum) in fishes.

The Nose.—The nose originates, like the eye and ear, in a depression of the superficial epiblast at each side of the fronto-nasal process (primary olfactory pit), which is at first in front of the cavity of the primitive mouth, and gradually extends backwards, into its roof (p. 846).

The olfactory bulbs of the brain lie in close relation with the roofs of the olfactory pits, and the olfactory nerves are outgrowths from special bipolar cells in the epithelium of the pit (see p. 736).

Development of the Alimentary Canal.

The alimentary canal in the earliest stages of its development consists of three parts—the fore- and hind-gut ending blindly at each end of the body, and a middle segment which communicates freely on its ventral surface with the cavity of the yolk-sac through the vitelline or omphalo-mesenteric duct.

From the fore-gut are formed the lower and back part of the mouth, the pharynx, œsophagus, stomach, and first and second parts of the duodenum; from the hind-gut, the lower end of the colon, the rectum, and the bladder. The upper and front part of the mouth, and the nasal chambers are developed from the stomadæal space (p. 847).

At the other end of the alimentary canal the anus is formed by an involution from the free surface, which at length opens into the hind-gut. When the depression from the free surface does not reach the intestine, the condition known as imperforate anus results. A similar condition may exist at the other end of the alimentary canal from the failure of the involution which forms the mouth, to meet the fore-gut.

The middle portion of the digestive canal becomes more and more closed in, till its wide communication with the yolk-sac becomes narrowed down to a small duct (vitelline). This duct usually completely disappears in the adult, but occasionally the proximal portion remains as a diverticulum from the intestine, Meckel's diverticulum. Sometimes a fibrous cord, attaching some part of the intestine to the umbilicus, remains to represent the vitelline duct. Such a cord has been known to cause, in after-life, strangulation of the bowel and death.

The alimentary canal lies in the form of a straight tube close beneath the vertebral column, but it gradually becomes long, convoluted, and divided into its special parts, stomach, small intestine, and large intestine (fig. 666), and at the same time comes to be suspended in the abdominal cavity by means of a lengthening mesentery formed from the splanchnopleur which attaches it to the vertebral column. The stomach originally has the same direction as the rest of the canal; its cardiac extremity being superior, its pylorus inferior. These changes of position may be readily understood from the accompanying figures (fig. 666).

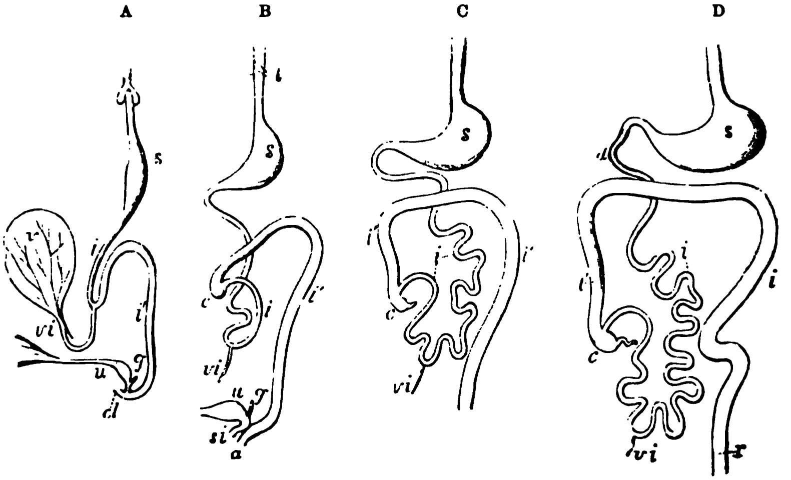

FIG. 666.—Outlines of the form and position of the alimentary canal in successive stages of its development. A, Alimentary canal, etc., in an embryo of four weeks; B, at six weeks; C, at eight weeks; l, the primitive lungs connected with the pharynx; s, the stomach; d, duodenum; i, the small intestine; i', the large intestine; c, the cæcum and vermiform appendage; r, the rectum; cl, in A, the cloaca; a, in B, the anus distinct from si, the sinus uro-genitalis; v, the yolk-sac, vi, the vitello-intestinal duct; u, the urinary bladder and urachus leading to the allantois; g, genital ducts. (Allen Thomson.)

Pancreas and Salivary Glands.—The principal glands in connection with the intestinal canal are the salivary glands, pancreas, and the liver. In mammalia, each salivary gland first appears as a simple canal with bud-like processes, lying in a mass of mesoblast, and communicating with the cavity of the mouth. As the development of the gland advances, the canal becomes more and more ramified (fig. 667). The submaxillary and sublingual glands and the pancreas are developed exactly in the same way, and their cells are derived from the hypoblast lining the fore-gut, while those of the parotid glands are formed from the epiblast lining the stomadæum. In both cases the blood-vessels and connective tissues are formed from the mesoblast into which the glandular structure grows.

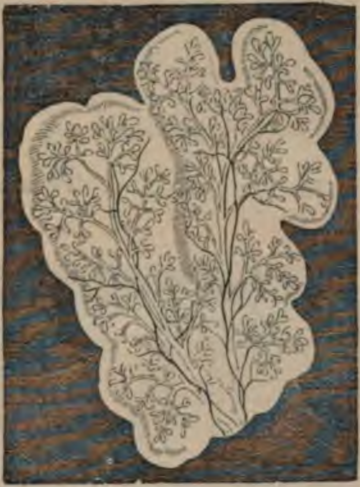
FIG. 667.—Lobules of the parotid with the salivary ducts, in the embryo of the sheep, at a somewhat advanced stage.

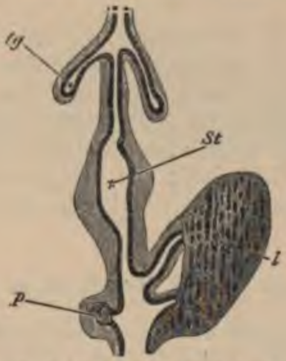

FIG. 668.—Diagram of part of digestive tract of a chick (4th day). The black line represents hypoblast, the outer shading mesoblast. *lg*, Lung diverticulum with expanded end forming primary lung-vesicle; *St*, stomach; *l*, two hepatic diverticula, with their terminations united by solid rows of hypoblast cells; *p*, diverticulum of the pancreas with the vesicular diverticula coming from it. (Gotte.)

The Liver.—The liver is developed by the protrusion of a part of the walls of the fore-gut, in the form of two conical hollow branches (figs. 668, 669). The inner portion of the cones consists of a number of solid cylindrical masses of cells, derived from the hypoblast, which become gradually hollowed by the formation of the hepatic ducts, and among which blood-vessels are rapidly developed. The secreting cells of the organ and the lining epithelium of the ducts are derived from the hypoblast; the connective tissue, and vessels from the mesoblast. The gall-bladder is developed as a diverticulum from the hepatic duct.

The *spleen* and *lymphatic glands* are developed from the mesoblast: the *thyroid* originates from the hypoblast; it grows as a diverticulum from the floor of the fore-gut, opposite the first clefts, and by two diverticula from the fourth visceral clefts. The hypoblastic cells form the lining epithelium of the vesicles; the stroma of the gland is formed by the surrounding mesoblast. The *thymus* is formed in a similar way from the third visceral clefts, and its hypoblastic cells form the corpuscles of Hassall; the lymphoid tissue by which they are invaded and ultimately surrounded is mesoblastic.

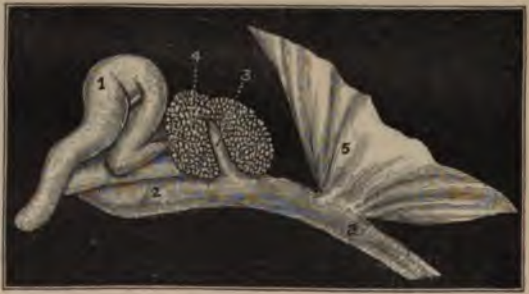

FIG. 669.—Rudiments of the liver on the intestine of a chick at the fifth day of incubation. 1, Heart; 2, intestine; 3, diverticulum of the intestine in which the liver (4) is developed; 5, part of the mucous layer of the germinal membrane. (Müller.)

Development of the Respiratory Apparatus.

The Lungs first appear as two small diverticula from a groove in the ventral wall of the fore-gut (figs. 668, 670).

The groove is gradually separated off to form the trachea and larynx, and the diverticula becomes the bronchi, whilst the dorsal part of the fore-gut in this region forms the œsophagus. These primary bronchial diverticula of the hypoblast of the alimentary canal send off secondary branches into the surrounding mesoblast, and these again give off tertiary branches, forming the air-cells. Thus we have the lungs formed: the epithelium lining the air-cells, bronchi, and trachea is derived from the hypoblast and all the rest of the lung-tissue, and of the tubes from the mesoblast.

The *diaphragm* is early developed as a partition of mesoblast dividing the original pleuro-peritoneal cavity into thoracic and abdominal serous cavities.

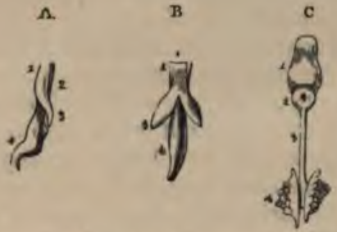

FIG. 670 illustrates the development of the respiratory organs. A is the œsophagus of a chick on the fourth day of incubation, with the rudiments of the trachea on the lung of the left side, viewed laterally; 1, the inferior wall of the œsophagus; 2, the upper portion of the same tube; 3, the rudimentary lung; 4, the stomach; B is the same object seen from below, so that both lungs are visible. C shows the tongue and respiratory organs of the embryo of a horse; 1, the tongue; 2, the larynx; 3, the trachea; 4, the lungs, viewed from the upper side. (After Rathke.)

Development of the Genito-urinary Apparatus.

In the early stage of the development of the urino-genital organs, the most striking thing seen is their resemblance to the segmental organs, or nephridia of worms. The subject was first worked out by Balfour in the elasmobranch fishes; we may therefore first describe what he found here, and then pass on to what occurs in mammals.

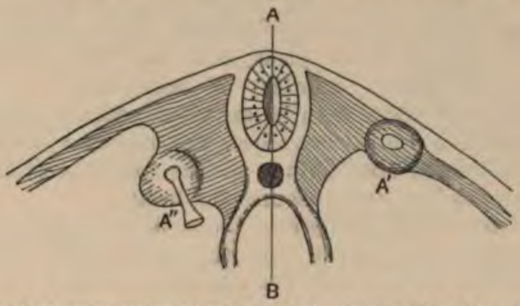

FIG. 671.—Diagram of transverse section of embryo dogfish. On the right of the middle line, A B, the primitive segmental tube (A′) is seen in transverse section; on the left side a later stage is represented; it here forms a well-marked projection into the pleuro-peritoneal cavity, and the section is represented as passing through the trumpet-shaped opening of the tube into that cavity (A″).

In the preceding diagram (fig. 671) we have a transverse section through the embryo in which the structures represented will be familiar from our previous studies. About the fifth segment a thickening in the mesoblast occurs, which grows backwards as a solid column of cells; this becomes hollow, and is seen in transverse section at A′; later on the hollow extends at one part into the pleuro-peritoneal cavity by a trumpet-shaped opening, and this is seen cut through at A″.

This duct is termed the *archinephros.* The prominence created by this duct grows into the pleuro-peritoneal cavity; and a number of convoluted tubes, one in each segment, open into the duct, which soon splits into two longitudinally; one division, the *pronephros* or *Müllerian duct* (fig. 672, M), has the original opening into the body cavity; the other convoluted tubes open into the other division; they become united together by connective tissue, and form a solid organ called the *Wolffian body,* or *mesonephros.* The duct is called the *mesonephric,* or *Wolffian duct* (fig. 672, W). The two ducts open into the *cloaca,* which also receives the hinder opening of the alimentary canal.

The tubules of the Wolffian body become more convoluted, and form the tubules of the primitive kidney; some of their original openings into the peritoneal cavity can be traced, even in the adult.

From the lower end of the Wolffian duct a protrusion or growth takes place, and this also becomes hollow, and a number of segmental tubes develop and form with it an organ similar to the Wolffian body; this is called the *metanephros,* and it forms the hind kidney, which represents the true kidney of the higher vertebrates (K, fig. 673); the *metanephric duct* becomes the ureter.

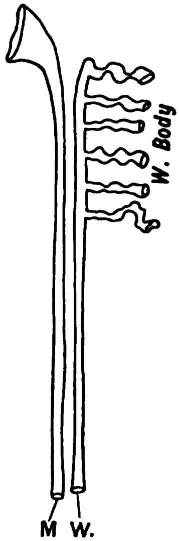

FIG. 672.—Diagram representing the splitting of the archinephros into Müllerian (M) and Wolffian (W) ducts.

In the female the Müllerian ducts become the oviducts, and, where they join, the uterus. In the male they disappear. The head or Wolffian kidney, and the hind or true kidney both execute renal functions in both sexes; but in the male, the Wolffian tubules apply themselves to the testis and constitute its efferent ducts; the main Wolffian duct becomes the vas deferens. Thus in fishes and amphibians, the semen passes through tubules which are also renal in function.

In the higher vertebrates the duct of the archinephros becomes the Wolffian duct, and the segmental tubules, which are rather more numerous than one to each segment, get bound into the Wolffian body. The Müllerian duct is not split off from this, but is formed separately by a longitudinal folding in of the pleuro-peritoneal cavity; the true kidney is formed in both sexes as before by a growth backwards from the Wolffian duct. The tubules are at first solid columns of cells which are subsequently hollowed out.

The Wolffian bodies, or temporary kidneys, as they may be termed, give place at an early period in the human fœtus to their successors, the permanent kidneys, which are developed behind them.

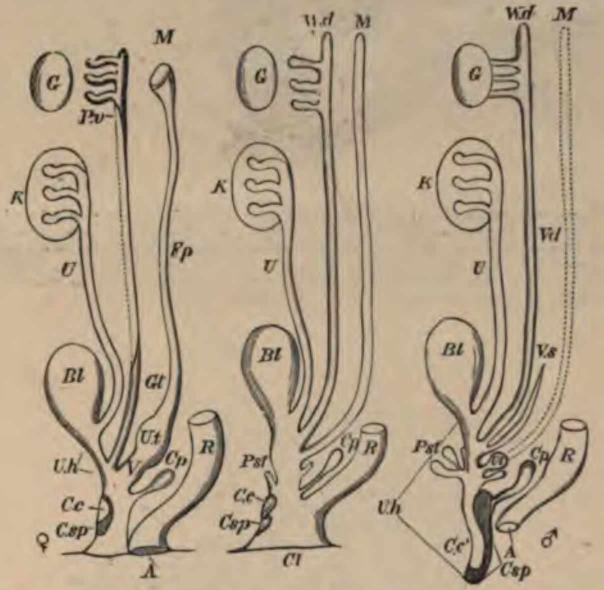

FIG. 673.—Diagram showing the relations of the female (the left-hand figure ♀) and of the male (the right-hand figure ♂) reproductive organs to the general plan (the middle figure) of these organs in the higher vertebrata (including man). *Cl*, Cloaca; *R*, rectum; *Bl*, urinary bladder; *U*, ureter; *K*, kidney; *Uh*, urethra; *G*, genital gland, ovary, or testis; *W*, Wolffian body; *W d*, Wolffian duct; *M*, Müllerian duct; *Pst*, prostate gland; *Cp*, Cowper's gland; *C.sp*, corpus spongiosum; *C.c*, corpus cavernosum.

In the female.—*V*, vagina; *Ut*, uterus; *Fp*, Fallopian tube; *Gt*, Gaertner's duct; *Pv*, parovarium; *A*, anus; *C.c*, *C.sp*, clitoris.

In the male.—*C.sp*, *C'.c'*, penis; *Ut*, uterus masculinis; *V s*, vesicula seminalis; *V d*, vas deferens. (Huxley.)

The Wolffian body loses all renal functions. In the male it applies itself to the testis, and is developed into the *vasa efferentia*, *coni vasculosi*, and *globus major* of the epididymis. Its *duct* forms the body and globus minor of the epididymis, the vas deferens, and the ejaculatory duct; the vesicula seminalis is a diverticulum from its lower part. In the female a relic of the Wolffian body persists as the *parovarium*, a functionless collection of tubules lined with ciliated epithelium near the ovary (see p. 821, fig. 613, *po*); in the male a similar relic is

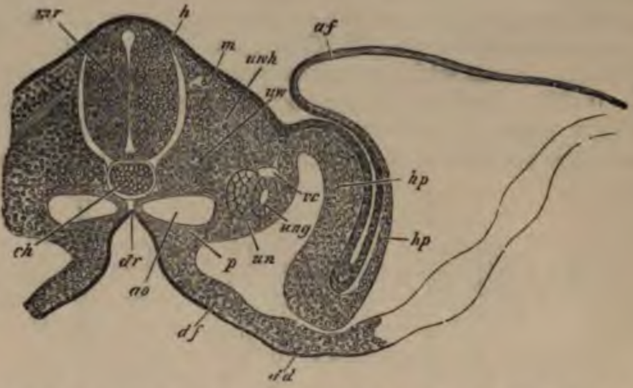

FIG. 674.—Transverse section of embryo chick (third day). *mr*, Rudimentary spinal cord; the primitive central canal has become constricted in the middle; *ch*, notochord; *uwh*, primordial vertebral mass; *m*, muscle-plate; *dr*, *df*, hypoblast and visceral layer of mesoblast lining groove, which is not yet closed in to form the intestines; *ao*, one of the primitive aortæ; *un*, Wolffian body; *ung*, Wolffian duct; *v c*, vena cardinalis; *h*, epiblast; *hp*, somatopleur and its reflection to form *a f*, amniotic fold; *p*, pleuro-peritoneal cavity. (Kölliker.)

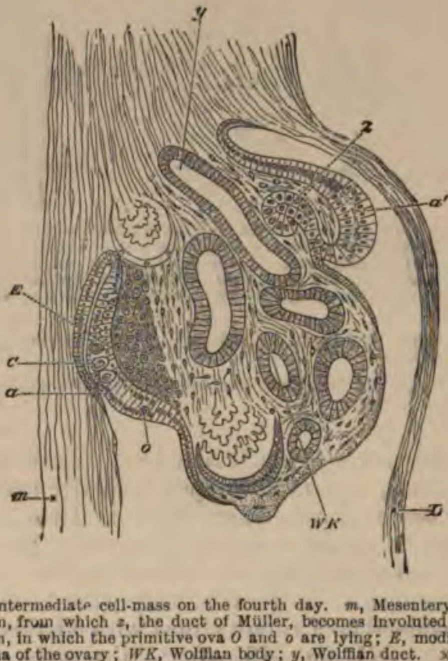

FIG. 675.—Section of intermediate cell-mass on the fourth day. *m*, Mesentery; *L*, somatopleur; *a'*, germinal epithelium, from which *z*, the duct of Müller, becomes involuted; *a*, thickened part of germinal epithelium, in which the primitive ova *O* and *o* are lying; *E*, modified mesoblast, which will form the stroma of the ovary; *WK*, Wolffian body; *y*, Wolffian duct. × 160. (Waldeyer.)

termed the *organ of Giraldès.* The lower end of the Wolffian duct may remain as the *duct of Gaertner,* which descends towards, and is lost upon, the anterior wall of the vagina.

The Fallopian tubes, the uterus, and the vagina are developed from the Müllerian ducts. The two Müllerian ducts are united below into a single cord, called the *genital cord,* and from this are developed the vagina, as well as the lower portion of the uterus; while the ununited portion of the duct on each side forms the upper part of the uterus and the Fallopian tube. In certain cases of arrested or abnormal development, these portions of the Müllerian ducts may not become fused together at their lower extremities, and there is left a cleft or horned condition of the upper part of the uterus resembling a condition which is permanent in certain of the lower animals (see fig. 676).

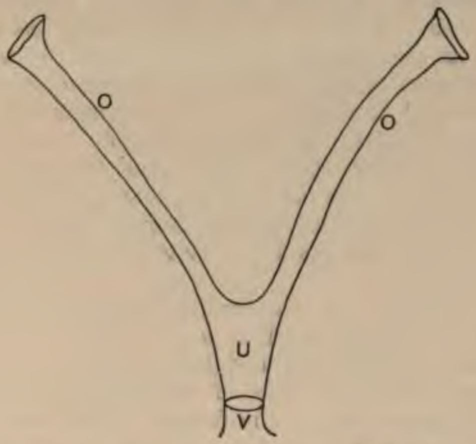

FIG. 676.—Diagram of two-horned uterus. The body of the uterus (U) is formed by the fusion of the two Müllerian ducts, the ununited portions of which form the oviducts, Fallopian tubes or horns of the uterus (O, O); V, vagina.

In the male, the Müllerian ducts have no special function, and are but slightly developed. The hydatid of Morgagni is the remnant of the upper part of the duct. The small prostatic pouch, *uterus masculinus,* or *sinus pocularis,* forms the atrophied remnant of the distal end of the genital cord, and is, therefore, the homologue of the vagina and uterus.

Between the Wolffian body and the mesentery, the mesoblast covering the ridge produced by the projecting Wolffian body is converted into a thick epithelium called the *germ epithelium* (see fig. 675). From this the reproductive gland (ovary or testis as the case may be) is developed.

The manner in which the ovary is formed is described in outline in Chapter LVIII. (p. 825); the testis is formed in a similar way, only the downgrowths of cells which become nests of cells to form ova and Graafian follicles in the female, become hollowed out as seminiferous tubules in the male.

For some time it is impossible to determine whether an ovary or testis will be developed; gradually, however, the special characters belonging to one of them appear, and in either case the organ soon begins to assume a relatively lower position in the body; the ovaries are thus ultimately placed in the pelvis, and the testicles descend into the scrotum; the testicle enters the internal inguinal ring in the seventh month of fœtal life, and completes its descent through the inguinal canal and external ring into the scrotum by the end of the eighth month. A pouch of peritoneum, the *processus vaginalis*, precedes it in its descent, and ultimately forms the tunica vaginalis or serous membrane of the organ; the communication between the tunica vaginalis and the cavity of the peritoneum is closed only a short time before birth. In its descent, the testicle or ovary of course retains the blood-vessels, nerves, and lymphatics, which were supplied to it while in the lumbar region, and which accompany it as it assumes a lower position in the body. Hence it is that these parts originate at so considerable a distance from the organ to which they are distributed.

The *gubernaculum testis* is a cord, partly fibrous, partly muscular, which extends while the testicle is yet high in the abdomen, from its lower part, through the abdominal wall (in the situation of the inguinal canal) to the front of the pubes and lower part of the scrotum. The homologue, in the female, of the gubernaculum testis is the *round ligament of the uterus*, which extends through the inguinal canal, from the outer and upper part of the uterus to the subcutaneous tissue in front of the symphysis pubis.

At a very early stage of fœtal life, the Wolffian ducts, ureters, and Müllerian ducts open into the lower extremity of the intestine, which constitutes for the time a common receptacle or *cloaca*. This opens to the exterior of the body through a part corresponding with the future anus, an arrangement which is permanent in reptiles, birds, and some of the lower mammalia. In the human fœtus, however, the intestinal portion of the cloaca is cut off from that which belongs to the urinary and generative organs; a separate passage or canal to the exterior of the body, belonging to these parts, is called the *sinus urogenitalis*. Subsequently, this canal is divided, by a process of division extending from before backwards or from above downwards, into a "pars urinaria" and a "pars genitalis." The former, continuous with the *urachus*, is converted into the urinary bladder.

The external parts of generation are at first the same in both sexes. The opening of the genito-urinary apparatus is, in both sexes, bounded by two folds of skin, whilst in front of it there is formed a penis-like body surmounted by the glans, with a cleft or furrow along its under surface. The borders of the furrows diverge posteriorly, running at the sides of the genito-urinary orifice internal to the cutaneous folds just mentioned. In the female, this body becoming retracted, forms the clitoris, and the margins of the furrow on its under surface are converted into the nymphæ, or labiæ minora, the labia majora pudendæ being constituted by the great cutaneous folds. In the male fœtus, the margins of the furrow at the under surface of the penis unite at about the fourteenth week, and form that part of the urethra which is included in the penis. The large cutaneous folds form the scrotum, and later receive the testicles. Sometimes the urethra is not closed, and the deformity called hypospadias then results. The appearance of hermaphroditism may, in these cases, be increased by the retention of the testes within the abdomen.

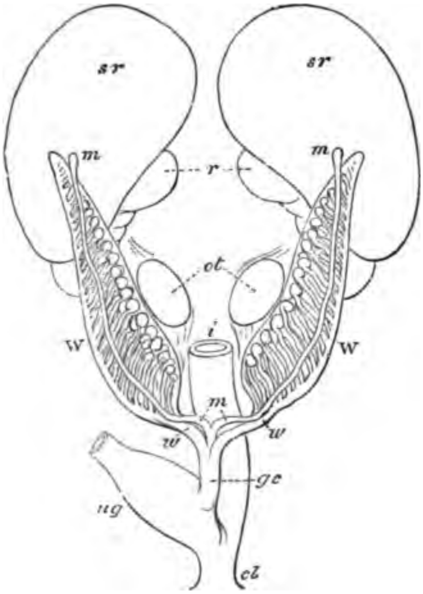

FIG. 677.—Diagram of the Wolffian bodies, Müllerian ducts and adjacent parts previous to sexual distinction, as seen from before. *sr*, The supra-renal bodies; *r*, the kidneys; *ot*, common blastema of ovaries or testicles; W, Wolffian bodies; *w*, Wolffian ducts; *mm*, Müllerian ducts; *g c*, genital cord: *ug*, sinus uro-genitalis; *i*, intestine; *cl*, cloaca. (Allen Thomson.)

The *supra-renal capsules* originate partly from the mesoblast and partly from certain special cells of the sympathetic ganglia, called chromofine cells, on account of the yellow colour they acquire when hardened with chromic salts. The chromofine cells form the medullary parts of the suprarenal bodies, and the cortex is developed from buds of mesoblastic cells separated from the peritoneum on the inner sides of the germinal ridges.

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